Access DB# 91769

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: ZINNA N. DAVIS Examiner #: 65429 Date: 4/17/2002
Art Unit: 1625 Phone Number 30 8-4679 Serial Number: 09/424,673
Mail Box and Bldg/Room Location: CM1 3A07 Results Format Preferred (circle): PAPER DISK E-MAIL
→ CM1 3D01

If more than one search is submitted, please prioritize searches in order of need.

****

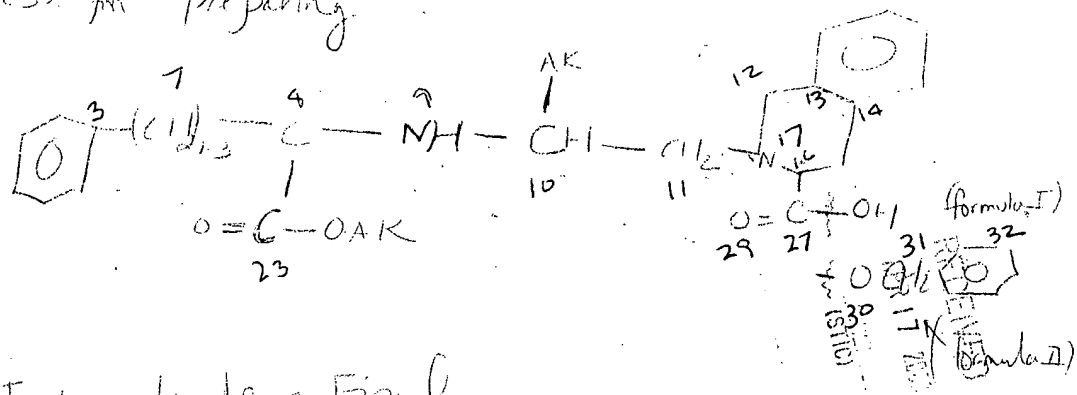
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: → Mongalvadje et al
Inventors (please provide full names): Process for preparing quinapril

Earliest Priority Filing Date: 5/29/1997

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Process for preparing



Intermediate & Final Product

Point of Contact:
Beverly Shears
Technical Info. Specialist
CM1 1E05 Tel: 308-4994

****

STAFF USE ONLY

Searcher: Beverly 4994
Searcher Phone #:
Searcher Location:
Date Searcher Picked Up:
Date Completed: 04-21-03
Searcher Prep & Review Time: 12
Exam Prep Time:
Time: 20

Type of Search

NA Sequence (#)
AA Sequence (#)
Structure (#)
Bibliographic
Litigation
Fulltext
Patent Family
Other

Vendors and cost where applicable

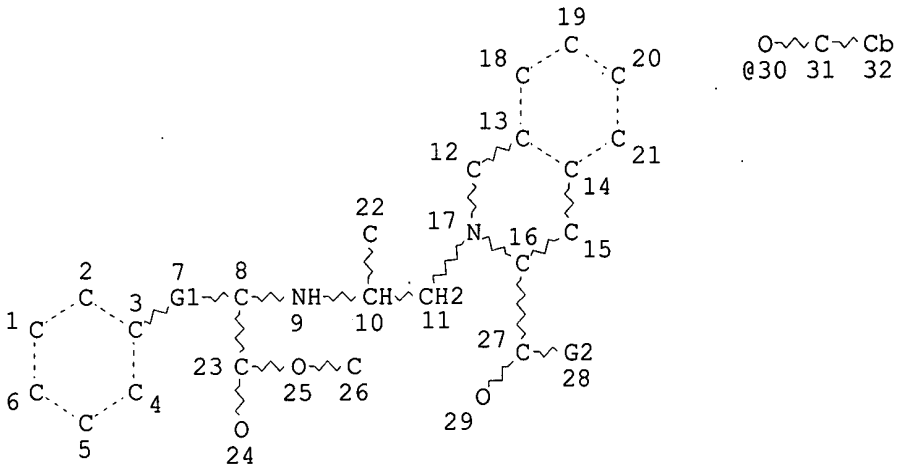
STN ✓
Dialog
Questel/Orbit
Dr.Link
Lexis/Nexis
Sequence Systems
WWW/Internet
Other (specify)

0 (8-01)

Northington-Davis
09/424673

(FILE 'REGISTRY' ENTERED AT 11:51:05 ON 21 APR 2003)

L5 STR



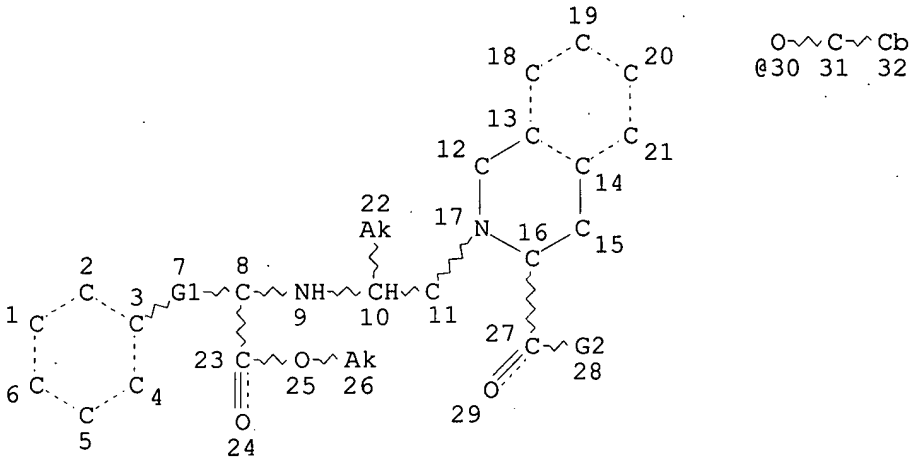
REP G1=(1-3) CH2
VAR G2=OH/30
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE
L7 0 SEA FILE=REGISTRY SSS FUL L5

100.0% PROCESSED 4015 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L8 STR



REP G1=(1-3) CH2
VAR G2=OH/30
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 32
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE
L10 67 SEA FILE=REGISTRY SSS FUL L8

100.0% PROCESSED 421 ITERATIONS 67 ANSWERS
SEARCH TIME: 00.00.01

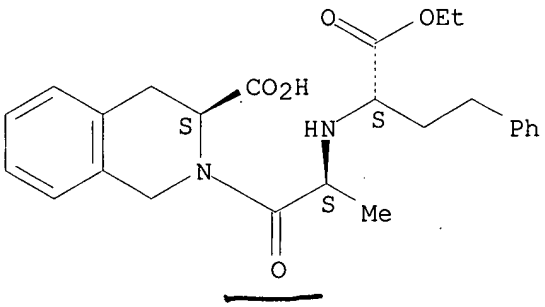
FILE 'HCAPLUS' ENTERED AT 12:01:30 ON 21 APR 2003
L11 25 S L10/P
L12 15 S L11 NOT (PY=>1997 OR PD=>19970529)

E1 THROUGH E38 ASSIGNED

L12 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:388940 HCAPLUS
DOCUMENT NUMBER: 123:111822
TITLE: ACE inhibitors as a template for the design of bradykinin B2 receptor antagonists
AUTHOR(S): Hoyer, Denton; Awad, Mohamed M. A.; Salvino, Joseph M.; Seoane, Peter R.; Dolle, Roland E.; Houck, Wayne T.; Sawutz, David G.
CORPORATE SOURCE: Department of Medicinal Chemistry, Sterling Winthrop Pharmaceutical Research Division, Collegeville, PA, 19426-0900, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1995), 5(4), 367-70
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Angiotensin converting enzyme (ACE) degrades both angiotensin II and bradykinin. Accordingly, it was hypothesized that ACE inhibitors can serve as models to design antagonists for the bradykinin receptor. The potent ACE inhibitor quinapril was modified to serve as a spacer sepg. two lipophilic pos. charges required for bradykinin binding. The synthesis and bradykinin receptor-binding activity of a series of antagonists (quinapril derivs.) based on this hypothesis were described.
IT **85441-61-8DP**, Quinapril, analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of quinapril derivs. as bradykinin B2 receptor antagonists)
RN 85441-61-8 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:572104 HCAPLUS
DOCUMENT NUMBER: 117:172104
TITLE: Methods for the synthesis of aminosuberic acid derivatives
INVENTOR(S): Hoffmann, Gerhard; Liedtke, Bernhard; Vollmer, Karl Otto
PATENT ASSIGNEE(S): Goedecke AG, Germany
SOURCE: Ger. Offen., 6 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4037960	A1	19920604	DE 1990-4037960	19901129

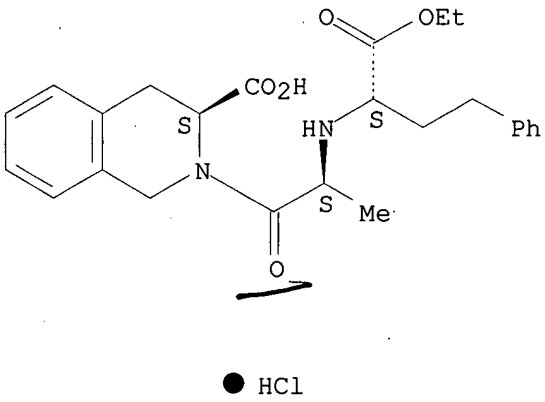
PRIORITY APPLN. INFO.: DE 1990-4037960 19901129
OTHER SOURCE(S): CASREACT 117:172104; MARPAT 117:172104
GI For diagram(s), see printed CA Issue.
AB Aminosuberic acid derivs. I (R1 = alkyl or alkenyl with up to 6

carbon atoms, C5-7-cycloalkyl, C5-7-cycloalkenyl, C7-12-cycloalkylalkyl, C6-10-aryl, C7-14-aralkyl, mono- or bicyclic heterocyclic group; R2 = aryl; R3 = C1-6-alkyl, C2-6-alkenyl, C7-14-aralkyl; Z forms a heterocyclic ring) were prepd. by the selective cleavage of PhCH2O2CCHR1NHCH(CO2R3)CH2COR2 with AlCl3, condensing the resulting HO2CCHR1NHCH(CO2R3)CH2COR2 with heterocyclic compd. II, and hydrogenating the resulting ketone III with H2, deuterium or tritium. Thus, (S,S)-PhCOCH2CH(CO2Et)-Ala-OCH2Ph was debenzylated with AlCl3 in the presence of anisole in CH2Cl2/MeNO2 to give 86% (S,S)-PhCOCH2CH(CO2Et)-Ala-OH, which was condensed with (S)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid benzyl ester by DCC/1-hydroxybenzotriazole in CH2Cl2 to give product IV (isolated as the HCl salt). IV was hydrogenated over Pd/C in the presence of HCl to give 88% tetrahydroisoquinoline V.HCl.

IT **82586-55-8P 143381-51-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and sapon. of)

RN 82586-55-8 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, monohydrochloride, (3S)- (9CI) (CA INDEX NAME)

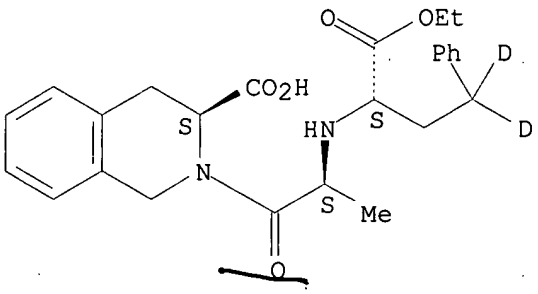
Absolute stereochemistry.



● HCl

RN 143381-51-5 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl-3,3-d2]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, monohydrochloride, [3S-[2[R*(R*)],3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

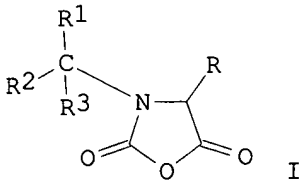


● HCl

L12 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:207829 HCAPLUS
DOCUMENT NUMBER: 114:207829
TITLE: Preparation of carboxyalkyl dipeptides useful as angiotensin-converting enzyme (ACE) inhibitors
INVENTOR(S): Oudenes, Jan; Schleicher, Richard Henry
PATENT ASSIGNEE(S): Pharma Investi S. A., Spain
SOURCE: Span., 10 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2004804	A6	19890201	ES 1987-2390	19870813

PRIORITY APPLN. INFO.: ES 1987-2390 19870813
OTHER SOURCE(S): MARPAT 114:207829
GI



I

AB R1R2R3CNHCHRCONR4CHR5COR6 [R, R1, R2 = H, alkyl, Ph, phenylalkyl, alkylphenyl, aminoalkyl, protected aminoalkyl; R3 = CO2H or its ester; R4 = H, alkyl; R5 = H, alkyl, Ph, phenylalkyl, alkylphenyl; R4R5 may form (un)substituted C4-9 monocyclic or fused bicyclic nucleus; R6 = OH, alkoxy, alkenyloxy, OPh, alkylsilyloxy, etc.], including such ACE inhibitors as enalapril, lisinopril, indolapril, ramipril, and quinapril, were prepd. by converting carboxylakyl R1R2R3CNHCHRCO2H to cyclic anhydrides I, reaction of I with

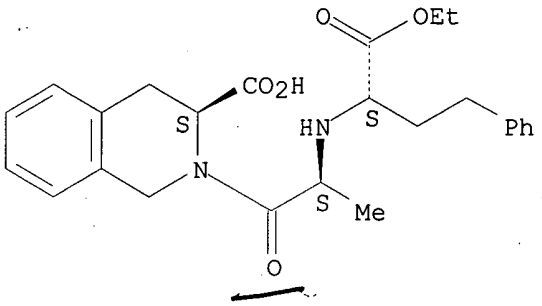
R4NHCHR5COR6, and optional deprotection, sapon. of R6, or salification. Thus, N-(1-S-ethoxycarbonyl-3-phenylpropyl)-L-alanine was treated with 1,1-carbonyldiimidazole in EtOAc at 20.degree., followed by L-proline. Two crystns. with maleic acid gave first imidazole maleate byproduct and then 77% 1-[N-[(S)-1-(ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline, i.e. enalapril maleate.

IT **85441-61-8P**, Quinapril
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, via cyclic anhydride)

RN 85441-61-8 HCAPLUS

CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:	1989:38911 HCAPLUS
DOCUMENT NUMBER:	110:38911
TITLE:	Preparation of crystalline quinapril, a known antihypertensive
INVENTOR(S):	Goel, Om P.; Krolls, Uldis
PATENT ASSIGNEE(S):	Warner-Lambert Co., USA
SOURCE:	U.S., 4 pp. CODEN: USXXAM
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4761479	A	19880802	US 1987-32209	19870330
AU 8812383	A1	19880929	AU 1988-12383	19880229
AU 605555	B2	19910117		
ZA 8801426	A	19891025	ZA 1988-1426	19880229
CA 1291999	A1	19911112	CA 1988-560594	19880304
EP 285992	A1	19881012	EP 1988-105131	19880329
EP 285992	B1	19910403		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 63258459	A2	19881025	JP 1988-73492	19880329
AT 62229	E	19910415	AT 1988-105131	19880329

PRIORITY APPLN. INFO.: US 1987-32209 19870330
EP 1988-105131 19880329

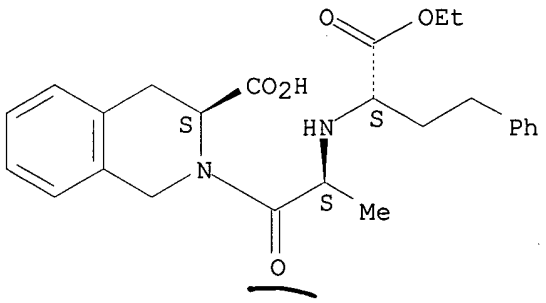
AB The title compd. (I) an angiotensin converting enzyme and antihypertensive agent is prepd. in a highly pure state. A soln. of I in glacial AcOH contg. HCl(g) was stirred for 2 h 20 min and was dild. with xylene; the process was repeated, the glossy solid dissolved in MeNC at 60.degree., and the product dried at 50.degree. under vacuum for 16 h to give 91.2% I-HCl.

IT **82586-55-8P**, Quinapril hydrochloride
RL: SPN (Synthetic preparation); PREP (Preparation)
(cryst., prepn. of)

RN 82586-55-8 HCAPLUS

CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, monohydrochloride, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L12 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1986:608744 HCAPLUS

DOCUMENT NUMBER: 105:208744

TITLE: Synthesis of novel angiotensin converting enzyme inhibitor quinapril and related compounds. A divergence of structure-activity relationships for non-sulfhydryl and sulfhydryl types

AUTHOR(S): Klutchko, Sylvester; Blankley, C. John; Fleming, Robert W.; Hinkley, Jack M.; Werner, Ann E.; Nordin, Ivan; Holmes, Ann; Hoefle, Milton L.; Cohen, David M.; et al.

CORPORATE SOURCE: Dep. Chem., Warner-Lambert/Parke-Davis Pharm. Res., Ann Arbor, MI, 48106, USA

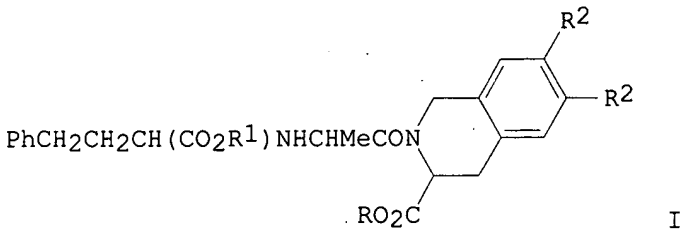
SOURCE: Journal of Medicinal Chemistry (1986), 29(10), 1953-61
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 105:208744

GI



I

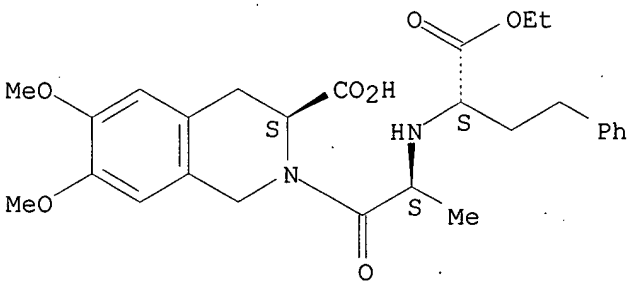
AB The synthesis and angiotensin-converting enzyme (ACE) inhibiting activities of quinapril (S,S,S)-I (R = R2 = H, R1 = Et), its active diacid (S,S,S)-I (R = R1 = R2 = H), and its dimethoxy analog (S,S,S)-I (R = H, R1 = Et, R2 = MeO) are reported. Thus, (S)-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid 1,1-dimethylethyl ester was acylated with (S,S)-PhCH2CH2CH(CO2Et)NHCHMeCO2H followed by hydrolysis of the product to give (S,S,S)-I (R = R2 = H, R1 = Et). These tetrahydro-3-isoquinolinecarboxylic acid derivs. possess in vitro potency and in vivo efficacy equiv. to that of enalapril. Sulfhydryl analogs with the same structural variation are also highly potent. In contrast, tetrahydro-1-isoquinolinecarboxylic acid and homologous isoindoline-1-carboxylic acid analogs show a striking divergence in potency between the two types, sulfhydryl analogs being essentially inactive, while non-sulfhydryl analogs are equipotent with the proline prototype. This is the first evidence suggesting that alternate binding modes may exist for the two major structural classes of small mol. ACE inhibitors.

IT **82586-52-5P 82637-57-8P 85441-61-8P**
89300-89-0P 103775-06-0P 103775-09-3P
103775-10-6P 103775-11-7P 103775-12-8P
103833-14-3P 103833-15-4P 103833-16-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and angiotensin converting enzyme inhibition activity of)

RN 82586-52-5 HCAPLUS

CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, monohydrochloride, (3S)- (9CI) (CA INDEX NAME)

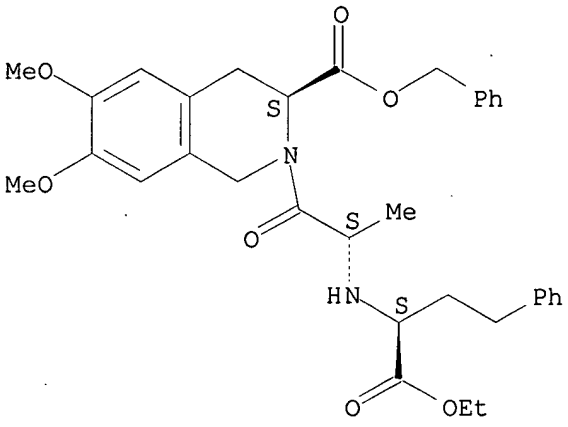
Absolute stereochemistry.



● HCl

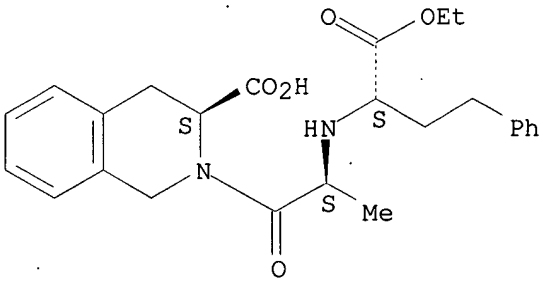
RN 82637-57-8 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, phenylmethyl ester, [3S-[2[R*(R*)],3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



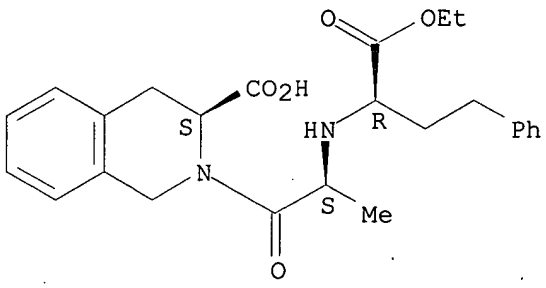
RN 85441-61-8 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 89300-89-0 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, monohydrochloride, [3S-[2[R*(S*)],3R*]]- (9CI) (CA INDEX NAME)

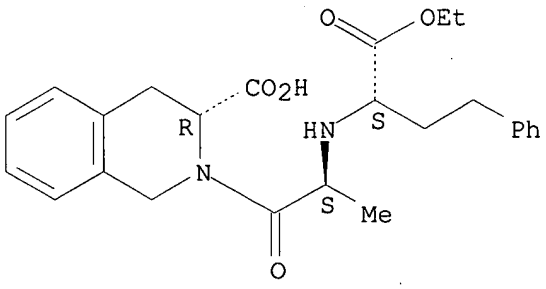
Absolute stereochemistry.



● HCl

RN 103775-06-0 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, monohydrochloride, [3R-[2[S*(S*)],3R*]]- (9CI) (CA INDEX NAME)

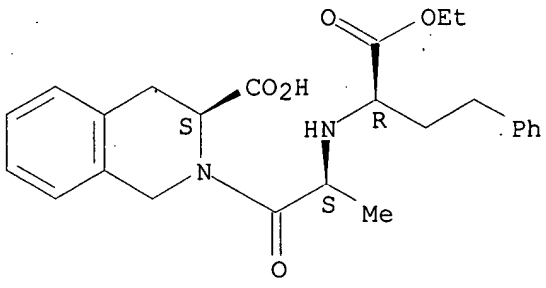
Absolute stereochemistry.



● HCl

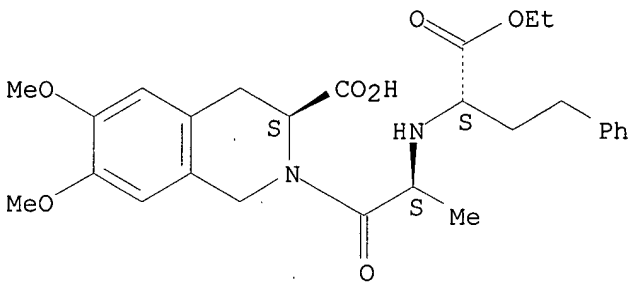
RN 103775-09-3 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, [3S-[2[R*(S*)],3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



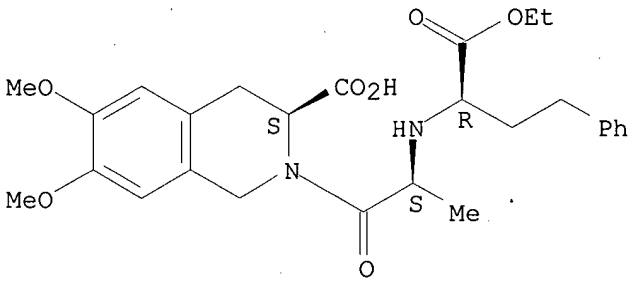
RN 103775-10-6 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



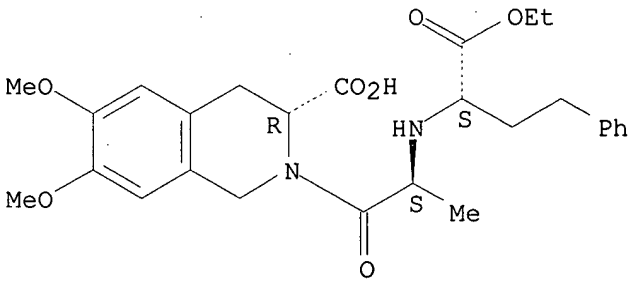
RN 103775-11-7 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, [3S-[2[R*(S*)],3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



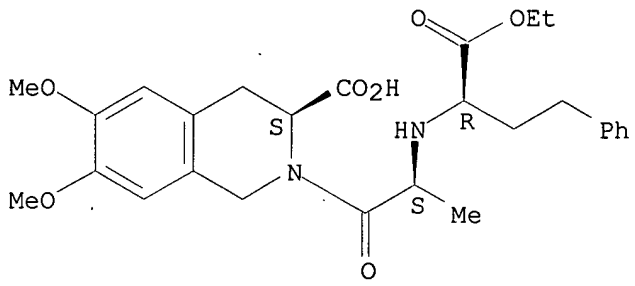
RN 103775-12-8 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, [3R-[2[S*(S*)],3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 103833-14-3 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, monohydrochloride, [3S-[2[R*(S*)],3R*]]- (9CI) (CA INDEX NAME)

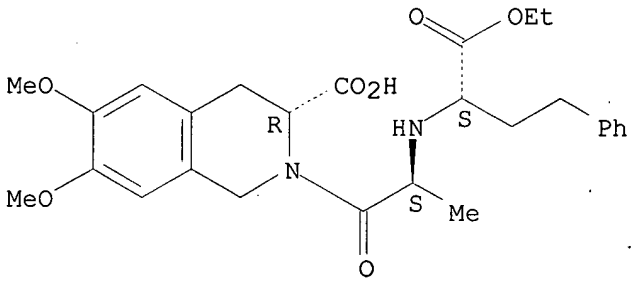
Absolute stereochemistry.



● HCl

RN 103833-15-4 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, monohydrochloride, [3R-[2[S*(S*)],3R*]]- (9CI) (CA INDEX NAME)

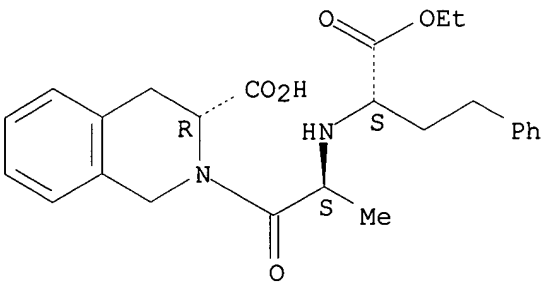
Absolute stereochemistry.



● HCl

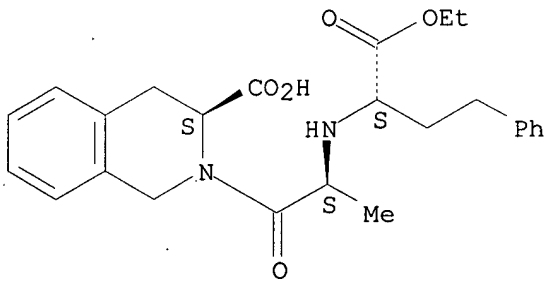
RN 103833-16-5 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, [3R-[2[S*(S*)],3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **82586-55-8P 82637-58-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and angiotensin-converting enzyme inhibition activity of)
RN 82586-55-8 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, monohydrochloride, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



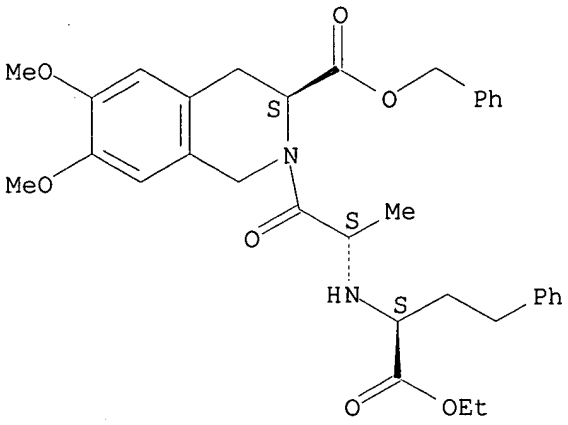
● HCl

RN 82637-58-9 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, phenylmethyl ester, (3S)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82637-57-8
CMF C34 H40 N2 O7

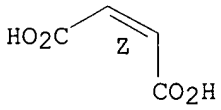
Absolute stereochemistry.



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.

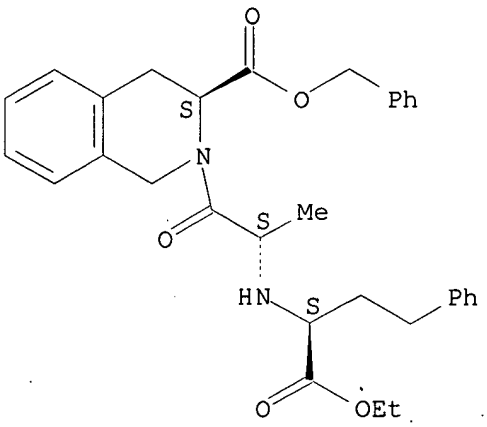


IT **82586-54-7P 103775-05-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and debenzylation of)
RN 82586-54-7 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, phenylmethyl ester, (3S)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82586-53-6
CMF C32 H36 N2 O5

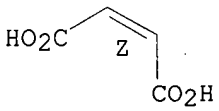
Absolute stereochemistry. Rotation (-).



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.

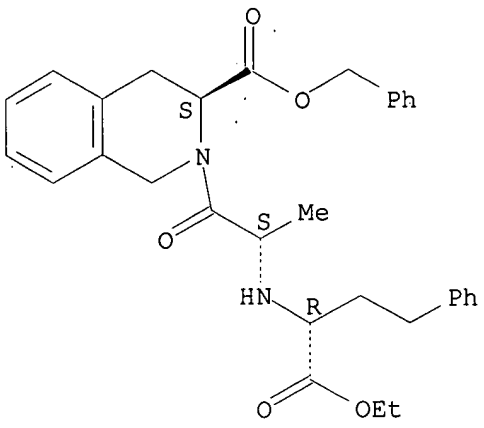


RN 103775-05-9 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1R)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, phenylmethyl ester, (3S)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 103775-04-8
CMF C32 H36 N2 O5

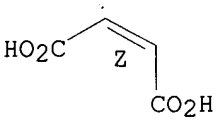
Absolute stereochemistry.



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



L12 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1985:560859 HCAPLUS
DOCUMENT NUMBER: 103:160859
TITLE: N-Alkylated dipeptides and their esters
INVENTOR(S): Teetz, Volker; Wissmann, Hans; Urbach, Hansjoerg
PATENT ASSIGNEE(S): Hoechst A.-G. , Fed. Rep. Ger.
SOURCE: Eur. Pat. Appl., 33 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

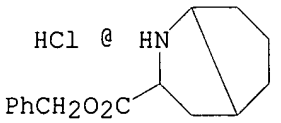
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 135182	A2	19850327	EP 1984-110678	19840907
EP 135182	A3	19860305		
EP 135182	B1	19880727		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
DE 3333454	A1	19850411	DE 1983-3333454	19830916
AT 35997	E	19880815	AT 1984-110678	19840907
HU 36145	O	19850828	HU 1984-3415	19840910
HU 201565	B	19901128		
FI 8403590	A	19850317	FI 1984-3590	19840913
FI 80464	B	19900228		

FI 80464	C	19900611			
CA 1338163	A1	19960312	CA 1984-463078	19840913	
DK 8404405	A	19850317	DK 1984-4405	19840914	
DK 164939	B	19920914			
DK 164939	C	19930201			
NO 8403662	A	19850318	NO 1984-3662	19840914	
NO 167743	B	19910826			
NO 167743	C	19911204			
AU 8433070	A1	19850321	AU 1984-33070	19840914	
AU 576782	B2	19880908			
JP 60089497	A2	19850520	JP 1984-191868	19840914	
JP 07098835	B4	19951025			
ZA 8407257	A	19850529	ZA 1984-7257	19840914	
ES 535917	A1	19851001	ES 1984-535917	19840914	
IL 72947	A1	19890228	IL 1984-72947	19840914	
US 5068351	A	19911126	US 1990-560004	19900727	

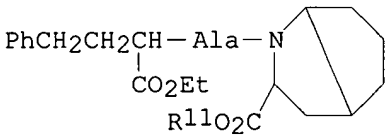
PRIORITY APPLN. INFO.:

DE 1983-3333454	19830916
EP 1984-110678	19840907
US 1984-650715	19840914
US 1986-943882	19861219
US 1988-178767	19880330
US 1989-403919	19890907

GI



II



III

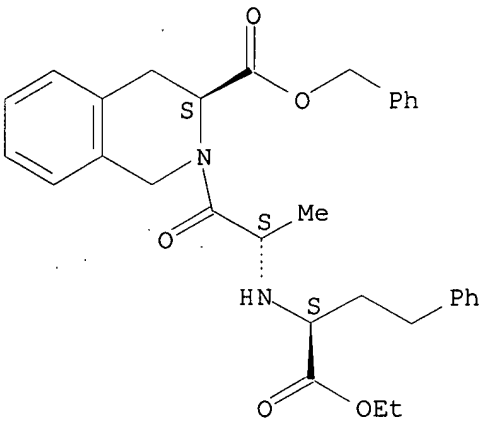
AB Title compds. R3O2CCHR4NR5COCHR1NHCH(CO2R2)(CH2)nR [n = 1, 2; R = H, (un)substituted C1-8 aliph., C3-9 alicyclic, C6-12 arom., C7-14 araliph., or C7-14 alicyclic aliph. residue, OR6, SR6 [R6 = (un)substituted C1-4 aliph., C6-12 arom., or heteroarom. residue]; R1 = H, (un)usbsituted C1-6 aliph., C3-9 alicyclic, C4-13 alicyclic aliph., C6-12 arom., C7-16 araliph., or heteroarom. residue, amino acid side chain; R2, R3 = H, (un)substituted C1-6 aliph., C3-9 alicyclic, C6-12 arom., or C7-16 araliph. residue; CHR4NR5 = C5-15 heterocyclic mono-, bi-, or tricyclic ring system] were prepd. via the condensation of HO2CCHR1NHCH(CO2R2)(CH2)nR with R3O2CCHR4NHR5 in the presence of phosphinic acid anhydrides R7R8P(O)OP(O)R9R10 (R7, R8, R9, R10 = alkyl or aralkyl). Thus, (S,S,S)-azabicyclo[3.3.0]octane II was condensed with (S)-PhCH2CH2CH(CO2Et)-(S)-Ala-OH by ethylmethylphosphinic acid anhydride in CH2Cl2 contg. Et3N to give peptide III (R11 = CH2Rh), which was debenzylated to give III (R1 = H). I inhibit angiotensin-converting enzyme and can be used as antihypertensives (no data).

IT **82586-53-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 82586-53-6 HCAPLUS

CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, phenylmethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

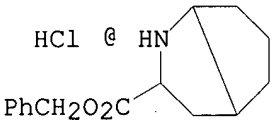


L12 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1985:560858 HCAPLUS
DOCUMENT NUMBER: 103:160858
TITLE: N-Alkylated dipeptides and their esters
INVENTOR(S): Urbach, Hansjoerg; Henning, Rainer; Wissmann, Hans; Teetz, Volker
PATENT ASSIGNEE(S): Hoechst A.-G. , Fed. Rep. Ger.
SOURCE: Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

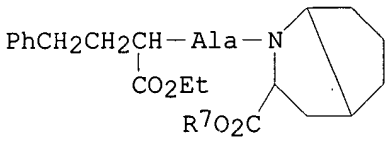
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 135181	A2	19850327	EP 1984-110677	19840907
EP 135181	A3	19860402		
EP 135181	B1	19900131		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
DE 3333455	A1	19850411	DE 1983-3333455	19830916
AT 49979	E	19900215	AT 1984-110677	19840907
HU 36140	O	19850828	HU 1984-3417	19840910
HU 198303	B	19890928		
FI 8403591	A	19850317	FI 1984-3591	19840913
FI 80275	B	19900131		
FI 80275	C	19900510		
CA 1338162	A1	19960312	CA 1984-463071	19840913
DK 8404404	A	19850317	DK 1984-4404	19840914
DK 166027	B	19930301		
DK 166027	C	19930712		
NO 8403663	A	19850318	NO 1984-3663	19840914
NO 167808	B	19910902		
NO 167808	C	19911218		
AU 8433071	A1	19850321	AU 1984-33071	19840914
AU 575585	B2	19880804		
JP 60089498	A2	19850520	JP 1984-191869	19840914
JP 07098836	B4	19951025		

ZA 8407259	A	19850529	ZA 1984-7259	19840914
ES 535918	A1	19851001	ES 1984-535918	19840914
IL 72946	A1	19900429	IL 1984-72946	19840914
US 5055591	A	19911008	US 1988-173024	19880323
PRIORITY APPLN. INFO.:			DE 1983-3333455	19830916
			EP 1984-110677	19840907
			US 1984-650714	19840914
			US 1986-943881	19861219

GI



II



III

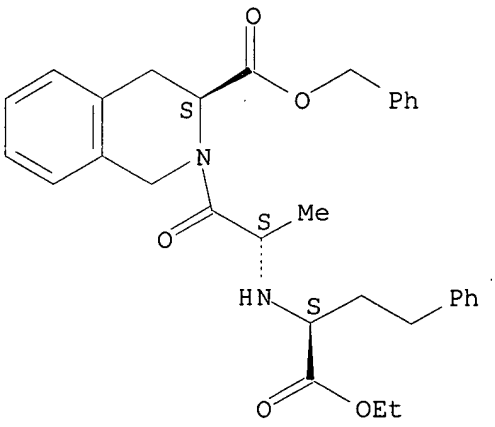
AB Title compds. R3O2CCHR4NR5COCHR1NHCH(CO2R2)(CH2)nR [I; n = 1, 2; R = H, (un)substituted C1-8 aliph., C3-9 alicyclic, C6-12 arom., C7-14 araliph., or C7-14 alicyclic aliph. residue, OR6, SR6 [R6 = (un)substituted C1-4 aliph., C6-12 arom., or heteroarom. residue]; R1 = H, (un)substituted C3-9 alicyclic, C4-13 alicyclic aliph., C6-12 arom., C7-16 araliph., or heteroarom. residue, amino acid side chain; R2, R3 = H, (un)substituted C1-6 aliph., C3-9 alicyclic, C6-12 arom., or C7-16 araliph. residue; CHR4NR5 = C5-15 heterocyclic mono-, bi-, or tricyclic ring system] were prepd. via the condensation of HO2CCHR1NHCH(CO2R2)(CH2)nR with R3O2CCHR4NHR5 in the presence of an alkanephosphoric acid anhydride. Thus, (S,S,S)-azabicyclo[3.3.0]octane II was condensed with (S)-PhCH2CH2CH(CO2Et)-(S)-Ala-OH by n-propanephosphonic acid anhydride in CH2Cl2 in the presence of N-ethylmorpholine to give peptide deriv. III (R7 = CH2Ph), which was debenzylated to give III (R7 = H) (all-S isomer). I inhibit angiotensin-converting enzyme and can be used as antihypertensives (no data).

IT **82586-53-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 82586-53-6 HCAPLUS

CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, phenylmethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L12 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1984:175294 HCAPLUS
DOCUMENT NUMBER: 100:175294
TITLE: Carboxyalkyl dipeptides and pharmaceutical compositions containing them
INVENTOR(S): Smith, Elizabeth M.; Witkowski, Joseph T.; Doll, Ronald J.; Gold, Elijah H.; Neustadt, Bernard R.; Yehaskel, Albert S.
PATENT ASSIGNEE(S): Schering Corp., USA
SOURCE: Eur. Pat. Appl., 134 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 88350	A1	19830914	EP 1983-102014	19830302
EP 88350	B1	19850220		
R: AT, BE, CH, DE, FR, IT, LI, LU, NL, SE				
US 4431645	A	19840214	US 1982-355639	19820308
US 4431644	A	19840214	US 1982-355638	19820308
ZA 8300362	A	19840926	ZA 1983-362	19830119
AT 11921	E	19850315	AT 1983-102014	19830302
NO 8300737	A	19830909	NO 1983-737	19830303
AU 8312035	A1	19830915	AU 1983-12035	19830303
AU 557795	B2	19870108		
GB 2117777	A1	19831019	GB 1983-5837	19830303
GB 2117777	B2	19850626		
ES 520261	A1	19840401	ES 1983-520261	19830303
DK 8301101	A	19830909	DK 1983-1101	19830304
JP 58162561	A2	19830927	JP 1983-35707	19830304
FI 8300752	A	19830909	FI 1983-752	19830307
HU 29605	O	19840228	HU 1983-781	19830307
HU 195520	B	19880530		
ZA 8301844	A	19840627	ZA 1983-1844	19830316

PRIORITY APPLN. INFO.: US 1982-355638 19820308
US 1982-355639 19820308

	US 1982-360532	19820322
	ZA 1983-362	19830119
	EP 1983-102014	19830302

OTHER SOURCE(S): CASREACT 100:175294

GI For diagram(s), see printed CA Issue.

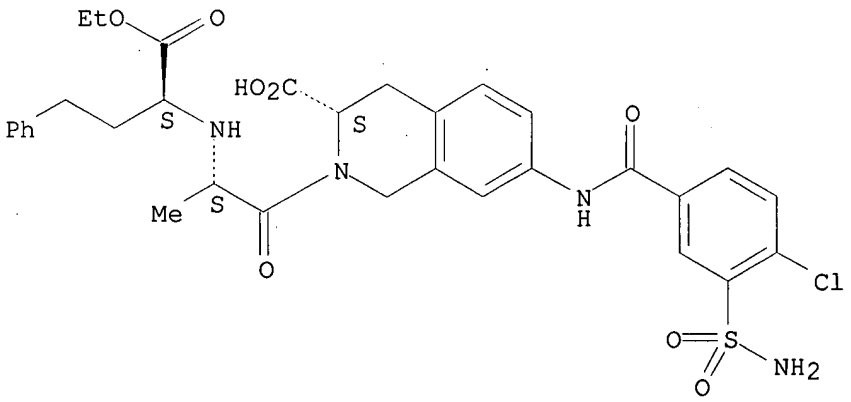
AB Title compds. RCH2CR1(CO2H)-NHCH[(CH2)nXR2]CO-X1-OH [R = alkyl, PhCH2, PhCH2O, PhCH2S, PhO, PhS; R1 = H, alkyl; X = S, R2 = substituted (3,4-dihydro-7-sulfamoyl-1,2,4-benzothiadiazin-3-yl 1,1-dioxide) methyl; X = NR3 (R3 = H, alkyl, Ph), R2 = sulfamoyl-substituted Bz, PhSO2, or benzyl; XR2 = sulfamoyl-substituted N-contg. heterocyclic ring; n = 1-6; X1 = (un)substituted Pro or related N-contg. heterocyclic amino acid residues] were prepd. as antihypertensives and agents for the treatment of congestive heart failure and glaucoma (no data). Thus, H-L-Lys(Z)-OH (Z = CO2CH2Ph) was treated with PhCH2CH2COCO2Et and NaBH3CN to give (S)-PhCH2CH2CH(CO2Et)-L-Lys(Z)-OH, which was condensed with indole I to give dipeptide II (R4 = Z, R5 = CH2Ph), which was deblocked by hydrogenolysis to give II (R4 = R5 = H), which was sulfonylated with 4-chloro-3-sulfamoylbenzenesulfonyl chloride to give title compd. III.

IT **89083-69-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 89083-69-2 HCAPLUS

CN 3-Isoquinolinecarboxylic acid, 7-[[3-(aminosulfonyl)-4-chlorobenzoyl]amino]-2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, [3S-[2[R*(R*)],3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2003 ACS

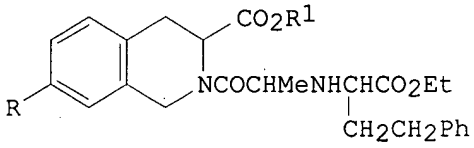
ACCESSION NUMBER:	1984:138974 HCAPLUS
DOCUMENT NUMBER:	100:138974
TITLE:	Tetrahydroisoquinoline derivatives
PATENT ASSIGNEE(S):	Takeda Chemical Industries, Ltd., Japan
SOURCE:	Jpn. Kokai Tokkyo Koho, 8 pp. CODEN: JKXXAF
DOCUMENT TYPE:	Patent
LANGUAGE:	Japanese
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

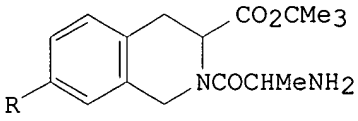
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 58188857	A2	19831104	JP 1982-69898	19820426

PRIORITY APPLN. INFO.: JP 1982-69898 19820426

GI



I



IV

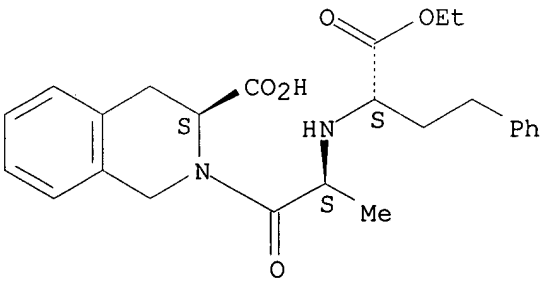
AB Tetrahydroisoquinoline derivs. I [R, R1, configuration = Me3C, Me3C, R (II); Me3C, Me3C, S (III); Me3C, H, R (HBr); Me3C, H, S (HBr); H, Me3C, R; H, Me3C, S; H, H, R (HCl); H, H, S (HCl)] were prepd. by reaction of IV with PhCH2CH2COCO2Et (V) optionally followed by hydrolysis. I had angiotensin-converting enzyme inhibitory and bradykinin-decompg. enzyme inhibitory activities and are useful as hypotensives (no data). Thus, a mixt. of (3S)-IV oxalate (R = Me3C) 3.2, AcOH 1.6, NaOAc 0.6, V 3.5, Mol. Sieve 3A 6, and Raney Ni 5 g in EtOH was hydrogenated to give 0.5 g II and 0.7 g III.

IT **82586-55-8P 89245-28-3P 89300-87-8P 89300-89-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 82586-55-8 HCAPLUS

CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, monohydrochloride, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

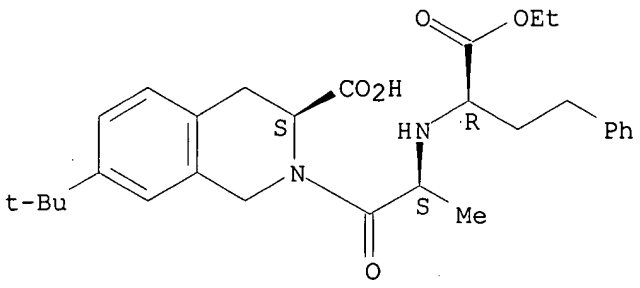


● HCl

RN 89245-28-3 HCAPLUS

CN 3-Isoquinolinecarboxylic acid, 7-(1,1-dimethylethyl)-2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, monohydrobromide, [3S-[2[R*(S*)],3R*]]- (9CI) (CA INDEX NAME)

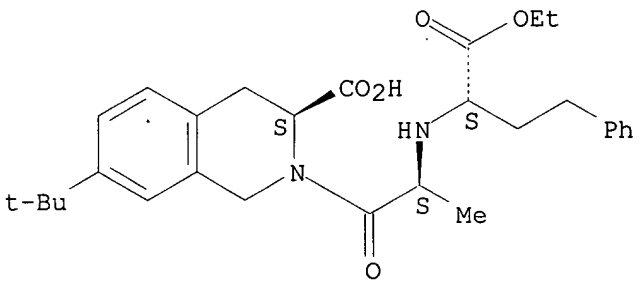
Absolute stereochemistry.



● HBr

RN 89300-87-8 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 7-(1,1-dimethylethyl)-2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, monohydrobromide, [3S-[2[R*(R*)],3R*]]- (9CI) (CA INDEX NAME)

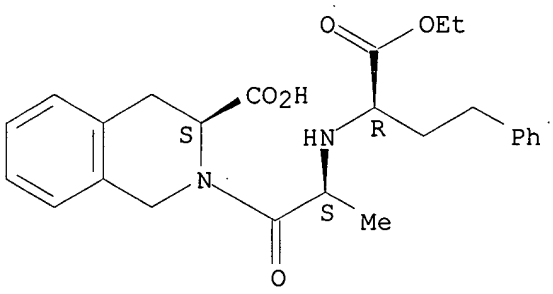
Absolute stereochemistry.



● HBr

RN 89300-89-0 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, monohydrochloride, [3S-[2[R*(S*)],3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

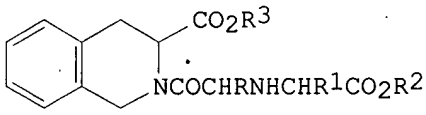


● HCl

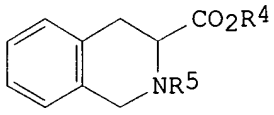
L12 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1983:216005 HCAPLUS
DOCUMENT NUMBER: 98:216005
TITLE: Tetrahydroisoquinolines
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 58021666	A2	19830208	JP 1981-120547	19810730

PRIORITY APPLN. INFO.: JP 1981-120547 19810730
GI



I

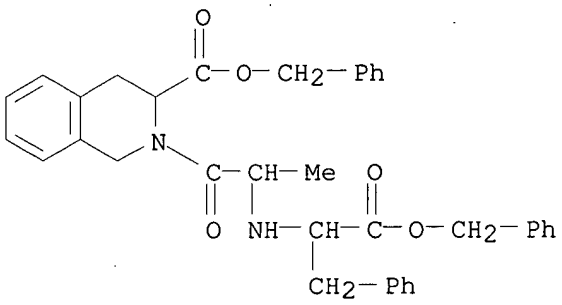


II

AB I (R = alkyl; R1 = alkyl, phenylalkyl; R2, R3 = H, alkyl, phenylalkyl) were prepd. by acylation of II (R4 = alkyl, phenylalkyl; R5 = H) with HO2CCHRX (X = halo) and condensation of the resulting II (R5 = COCHRX) with H2NCHR1CO2R6 (R6 = alkyl, phenylalkyl) followed by deesterification and optional esterification. Thus, a mixt. of 8.0 g II (R4 = CH2Ph, R5 = COCHBrMe), prepd. from HO2CCHMeBr and II (R4 = CH2Ph, R5 = H), 20 mL P(NMe2)3, 2.8 g K2CO3, and 5.1 g L-H-Phe-OCH2Ph was stirred at room temp. for 1 day to give 4.8 g .alpha.- and 1.0 g .beta.-stereoisomers of I (R = Me, R1 = R2 = R3 = CH2Ph). Hydrogenation of 2.0 g the .alpha.-stereoisomer over Pd/C gave 1.0 g I (R2 = R3 = H). I inhibited angiotensin-converting enzyme in vitro.

IT **85892-46-2P**

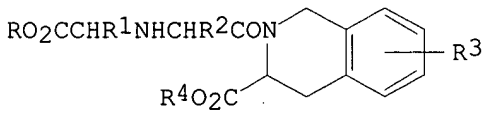
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antihypertensive agent)
RN 85892-46-2 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 1,2,3,4-tetrahydro-2-[1-oxo-2-[[2-oxo-2-(phenylmethoxy)-1-(phenylmethyl)ethyl]amino]propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



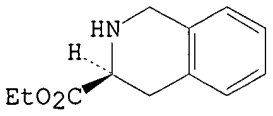
L12 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1983:179903 HCAPLUS
DOCUMENT NUMBER: 98:179903
TITLE: Isoquinolinecarboxylic acid derivatives and pharmaceutical composition containing them
INVENTOR(S): Patchett, Arthur A.; Wu, Mu Tsu
PATENT ASSIGNEE(S): Merck and Co., Inc. , USA
SOURCE: Eur. Pat. Appl., 30 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 65301	A1	19821124	EP 1982-104291	19820517
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
JP 58004770	A2	19830111	JP 1982-82521	19820518
PRIORITY APPLN. INFO.:			US 1981-264880	19810518
			US 1982-362082	19820329

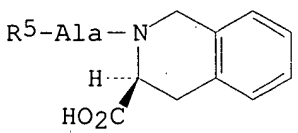
GI



I



II



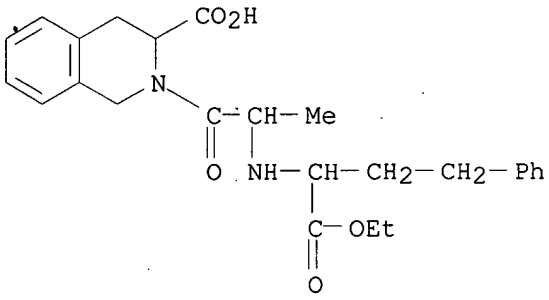
III

AB Title compds. I [R, R4 = H, alkyl, aralkyl; R1 = C1-10 alkyl, substituted C1-6 alkyl, (un)substituted aralkyl or heteroaralkyl; R2 = H, (un)substituted C1-6 alkyl; R3 = H, halo, alkoxy] were prepd. as angiotensin-converting enzyme inhibitors and antihypertensives (no data). Thus, Z-Ala-OH (Z = PhCH2O2C) was condensed with isoquinoline II by DCC to give a product, which was sapond. and then Z-deblocked by HBr/HOAc to give alanylisoquinoline III (R5 = H), which was condensed with PhCH2CH2COCO2Et in the presence of NaBH3CN to III [R5 = CH(CO2Et)CH2CH2Ph].

IT **82768-84-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and sapon. of)

RN 82768-84-1 HCAPLUS

CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)

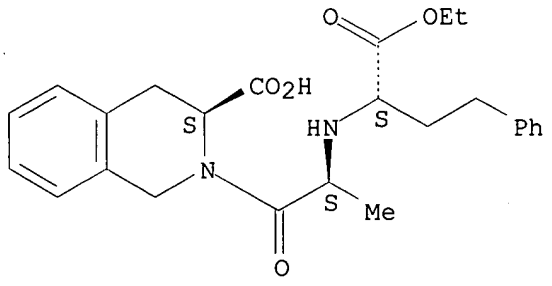


IT **85441-61-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 85441-61-8 HCAPLUS

CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

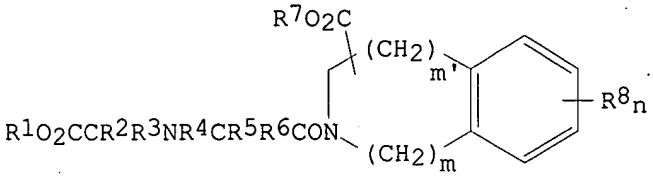


L12 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1983:89930 HCAPLUS

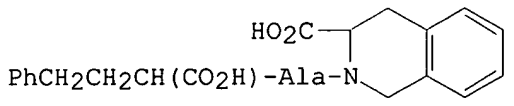
DOCUMENT NUMBER: 98:89930
TITLE: Amidoamino acids and pharmaceutical preparations containing them
INVENTOR(S): Suh, John T.; Barton, Jeffrey N.; Regan, John R.
PATENT ASSIGNEE(S): USV Pharmaceutical Corp., USA
SOURCE: Belg., 27 pp.
CODEN: BEXXAL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 892552	A1	19820920	BE 1982-207610	19820318
IN 156096	A	19850511	IN 1982-CA265	19820308
NL 8201066	A	19821018	NL 1982-1066	19820315
IL 65247	A1	19870731	IL 1982-65247	19820315
SE 8201654	A	19820920	SE 1982-1654	19820316
AU 8281584	A1	19820923	AU 1982-81584	19820316
AU 558451	B2	19870129		
GB 2095252	A	19820929	GB 1982-7770	19820317
GB 2095252	B2	19850417		
DE 3209708	A1	19821021	DE 1982-3209708	19820317
ES 510498	A1	19830801	ES 1982-510498	19820317
NO 8200903	A	19820920	NO 1982-903	19820318
DK 8201209	A	19820920	DK 1982-1209	19820318
JP 57165355	A2	19821012	JP 1982-41801	19820318
ZA 8201833	A	19830126	ZA 1982-1833	19820318
CH 658455	A	19861114	CH 1982-1691	19820318
FI 8200974	A	19820920	FI 1982-974	19820319
FR 2502149	A1	19820924	FR 1982-4738	19820319
FR 2502149	B1	19850118		
ES 521030	A1	19840516	ES 1983-521030	19830316
ES 521031	A1	19841201	ES 1983-521031	19830316

PRIORITY APPLN. INFO.: US 1981-245407 19810319
GI



I



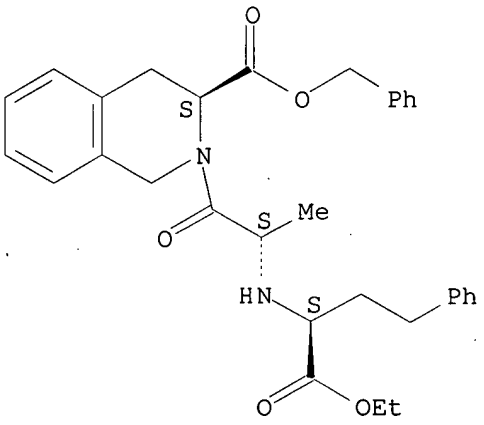
II

AB Amino acid-substituted tetrahydroisoquinoline derivs. and related compds. I [R1, R7 = H, alkyl, phenylalkyl; R2-R6 = H or (un)substituted alkyl, alkenyl, alkynyl, aryl, cycloalkyl, or

heterocyclyl; R8 = alkyl, NO2, amino, OH, halo, CF3, etc.; m = 0-2, m' = 1-3, n = 0-4] and their salts were prepd. The products are useful as antihypertensives (no data). Thus, Me L-1,2,3,4-tetrahydro-3-isoquinolinecarboxylate HCl salt was acetylated with PhCH2O2C-Ala-OH and the product deprotected and then treated with PhCH2CH2COCO2H followed by redn. with NaBH3CN to give II.

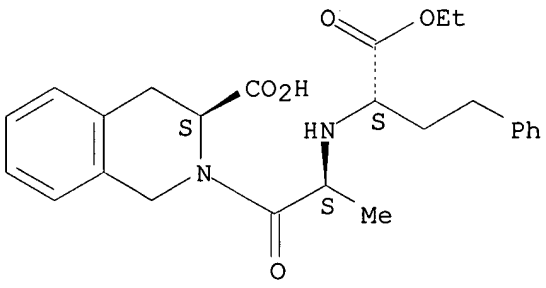
IT **82586-53-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydrogenolysis of)
RN 82586-53-6 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, phenylmethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **82586-55-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 82586-55-8 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, monohydrochloride, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L12 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1983:34598 HCAPLUS
DOCUMENT NUMBER: 98:34598
TITLE: Substituted acyl derivatives of 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acids
INVENTOR(S): Hoefle, Milton L.; Klutchko, Sylvester
PATENT ASSIGNEE(S): Warner-Lambert Co. , USA
SOURCE: U.S., 8 pp. Cont.-in-part of U.S. Ser. No. 193,767, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4344949	A	19820817	US 1981-236397	19810220
ZA 8106332	A	19820929	ZA 1981-6332	19810911
IL 63806	A1	19850228	IL 1981-63806	19810911
AU 8175416	A1	19820506	AU 1981-75416	19810917
AU 551239	B2	19860424		
FI 8103033	A	19820404	FI 1981-3033	19810930
FI 78690	B	19890531		
FI 78690	C	19890911		
DK 8104360	A	19820404	DK 1981-4360	19811001
DK 163120	B	19920120		
DK 163120	C	19920615		
EP 49605	A1	19820414	EP 1981-304541	19811001
EP 49605	B1	19870318		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
JP 57088164	A2	19820601	JP 1981-154900	19811001
JP 03016359	B4	19910305		
EP 96157	A2	19831221	EP 1983-102092	19811001
EP 96157	A3	19840912		
EP 96157	B1	19870325		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 25974	E	19870415	AT 1981-304541	19811001
AT 26120	E	19870415	AT 1983-102092	19811001

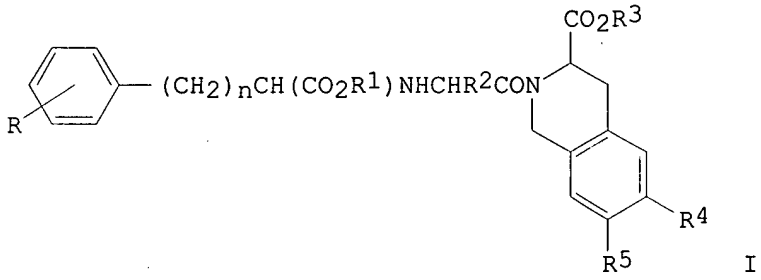
NO 8103359	A	19820405	NO 1981-3359	19811002
NO 159017	B	19880815		
NO 159017	C	19881123		
ES 505960	A1	19821216	ES 1981-505960	19811002
DD 201787	A5	19830810	DD 1981-233850	19811002
HU 25890	O	19830829	HU 1981-2864	19811002
HU 183602	B	19840528		
SU 1148560	A3	19850330	SU 1981-3340548	19811002
US 4532342	A	19850730	US 1982-386375	19820608
AU 8652991	A1	19860717	AU 1986-52991	19860204
AU 563683	B2	19870716		
FI 8801985	A	19880427	FI 1988-1985	19880427
FI 79839	B	19891130		
FI 79839	C	19900312		
CA 1331614	A1	19940823	CA 1992-616411	19920623
CA 1331615	A1	19940823	CA 1992-616412	19920623

PRIORITY APPLN. INFO.:

US 1980-193767	19801003
US 1981-236397	19810220
CA 1981-387002	19810930
FI 1981-3033	19810930
EP 1981-304541	19811001

OTHER SOURCE(S): CASREACT 98:34598

GI



I

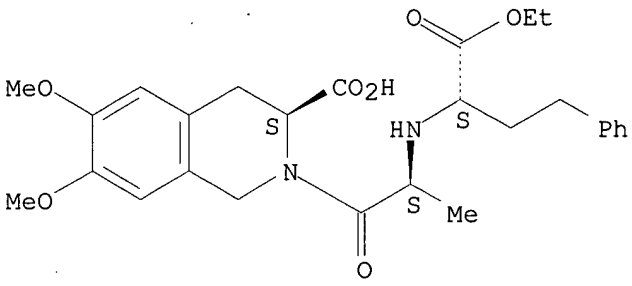
AB Antihypertensive acyltetrahydroisquinolinecarboxylates I (R = H, F, Cl, Br, alkyl, alkoxy, HO, H2N; R1 = H, alkyl; R2 = H, alkyl, PhCH2; R3 = H, alkyl, phenylalkyl; R4, R5 = H, alkyl, alkoxy, alkylthio, alkylsulfonyl, HO; R4R5 = OCH2O; n = 0-3) were prepd. Thus, substitution reaction of H-Ala-OCMe3 with Ph(CH2)2CHBrCO2Et and subsequent debutylation and sepn. of diastereoisomers gave (S,S)-PhCH2CH2CH(CO2Et)-Ala-CO2H, which was condensed with benzyl (S)-1,2,3,4-tetrahydro-6,7-dimethoxy-3-isoquinolinecarboxylate to give (S,S,S)-I (R = H, R1 = Et, R2 = Me, R3 = PhCH2, R4 = R5 = MeO). I inhibited angiotensin converting enzyme with IC50 2.8 .times. 10-9-2.0 .times. 10-6 M.

IT **82586-52-5P 82586-55-8P 82637-58-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and angiotensin-converting enzyme inhibiting activity of)

RN 82586-52-5 HCAPLUS

CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, monohydrochloride, (3S)- (9CI) (CA INDEX NAME)

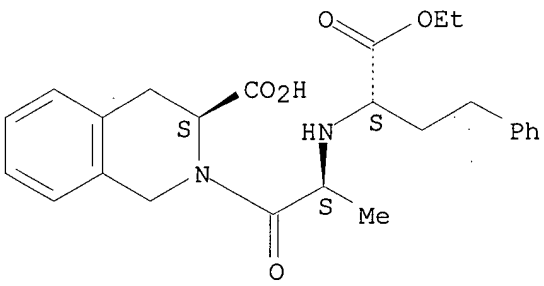
Absolute stereochemistry.



● HCl

RN 82586-55-8 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, monohydrochloride, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



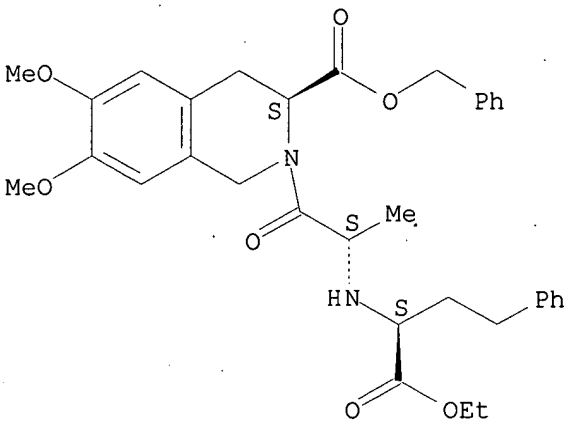
● HCl

RN 82637-58-9 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, phenylmethyl ester, (3S)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82637-57-8
CMF C34 H40 N2 O7

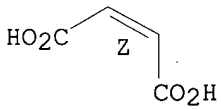
Absolute stereochemistry.



CM 2

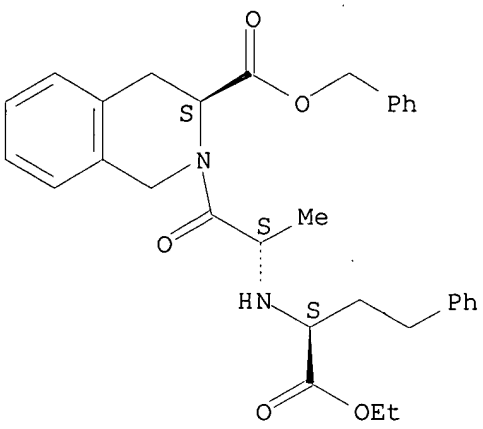
CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



IT **84048-96-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydrogenolysis of)
RN 84048-96-4 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, phenylmethyl ester, monohydrochloride, [3S-[2[R*(R*)],3R*]]- (9CI) (CA INDEX NAME)

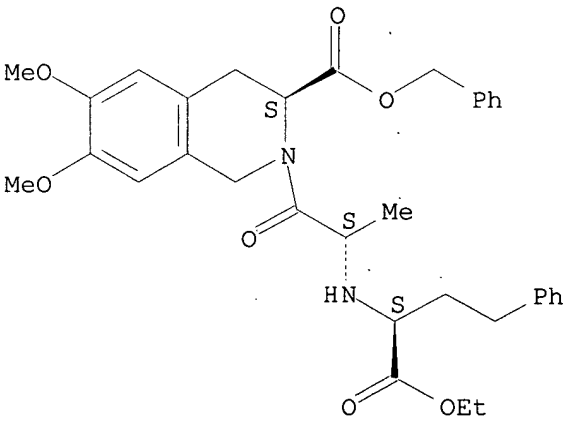
Absolute stereochemistry. Rotation (-).



● HCl

IT **82637-57-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 82637-57-8 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, phenylmethyl ester, [3S-[2[R*(R*)],3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1982:492759 HCAPLUS
DOCUMENT NUMBER: 97:92759
TITLE: Amino acid derivatives, compositions containing them and their use
INVENTOR(S): Geiger, Rolf; Teetz, Volker; Urbach, Hansjoerg; Schoelkens, Bernward; Henning, Rainer
PATENT ASSIGNEE(S): Hoechst A.-G. , Fed. Rep. Ger.

SOURCE: Eur. Pat. Appl., 196 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 46953	A2	19820310	EP 1981-106535	19810822
EP 46953	A3	19820505		
EP 46953	B1	19891206		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
DE 3032709	A1	19820429	DE 1980-3032709	19800830
DE 3118191	A1	19821125	DE 1981-3118191	19810508
EP 278530	A2	19880817	EP 1988-102408	19810822
EP 278530	A3	19890802		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
EP 328160	A1	19890816	EP 1989-105371	19810822
EP 328160	B1	19940504		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 48415	E	19891215	AT 1981-106535	19810822
AT 105301	E	19940515	AT 1989-105371	19810822
ES 504955	A1	19820816	ES 1981-504955	19810825
FI 8102652	A	19820301	FI 1981-2652	19810827
FI 90072	B	19930915		
FI 90072	C	19931227		
HU 27874	O	19831128	HU 1981-2478	19810827
HU 189531	B	19860728		
DK 8103835	A	19820301	DK 1981-3835	19810828
DK 169382	B1	19941017		
NO 8102933	A	19820301	NO 1981-2933	19810828
AU 8174718	A1	19820311	AU 1981-74718	19810828
AU 544756	B2	19850613		
ZA 8105988	A	19820825	ZA 1981-5988	19810828
IL 63683	A1	19880331	IL 1981-63683	19810828
JP 01048918	B4	19891020	JP 1981-134401	19810828
ES 505604	A1	19821116	ES 1981-505604	19810918
ES 505605	A1	19821116	ES 1981-505605	19810918
US 5158959	A	19921027	US 1983-565900	19831227
US 5162362	A	19921110	US 1983-565887	19831227
AU 8779284	A1	19880204	AU 1987-79284	19871001
AU 599151	B2	19900712		
JP 01125398	A2	19890517	JP 1988-209625	19880825
JP 06078355	B4	19941005		
AU 8936625	A1	19891005	AU 1989-36625	19890620
AU 627741	B2	19920903		
JP 04217994	A2	19920807	JP 1991-77208	19910318
JP 07121955	B4	19951225		
FI 90069	B	19930915	FI 1991-4555	19910927
FI 90069	C	19931227		
FI 90532	B	19931115	FI 1991-4554	19910927
FI 90532	C	19940225		
US 5401766	A	19950328	US 1994-208443	19940309

PRIORITY APPLN. INFO.:

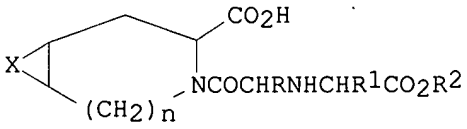
DE 1980-3032709	19800830
DE 1981-3118191	19810508
EP 1981-106535	19810822
EP 1989-105371	19810822

Searcher : Shears 308-4994

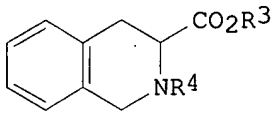
US 1981-297191 19810828

OTHER SOURCE(S): CASREACT 97:92759

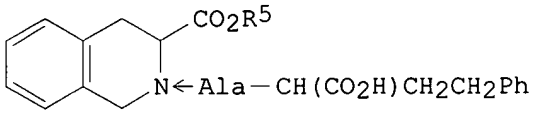
GI



I



II



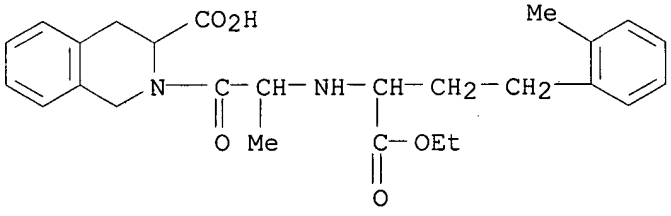
III

AB Amino acid derivs. I (X = fused benzene or cyclohexane ring; R, R1 = alkyl, alkenyl, cycloalkyl, cycloalkenyl, cycloalkylalkyl, aryl, partially hydrogenated aryl, aralkyl, heterocyclic residue; R2 = H, alkyl, alkenyl, aralkyl; n= 0, 1) were prepd. as long-lasting antihypertensives (no data). Thus, tetrahydroisoquinoline II (R3 = R4 = H) was treated with ZCl (Z = PhCH2O2C) to give II (R3 = H, R4 = Z), which was esterified with Me3COH by DCC in CH2Cl2 contg. 4-(dimethylamino)pyridine to give 97% II (R3 = CMe3, R4 = Z), which was Z-deblocked by hydrogenolysis and then condensed with Z-Ala-OH by DCC/1-hydroxybenzotriazole to give II (R3 = CMe3, R4 = Z-Ala). The latter was Z-deblocked by hydrogenolysis to give II (R = CMe3, R4 = Ala), which condensed with PhCH2CH2COCO2H and was then reduced with NaBH3CN to give isoquinoline III (R5 = CMe3), which was debutylated by CF3CO2H to give III (R5 = H).

IT **82713-51-7P 82713-52-8P 82713-55-1P**
82713-58-4P 82713-62-0P 82713-63-1P
82713-64-2P 82713-65-3P 82713-66-4P
82713-90-4P 82714-28-1P 82714-29-2P
82714-32-7P 82768-84-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 82713-51-7 HCAPLUS

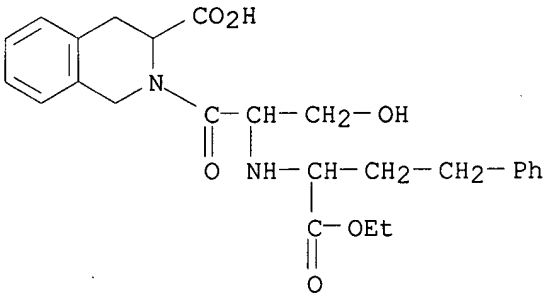
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-(2-methylphenyl)propyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



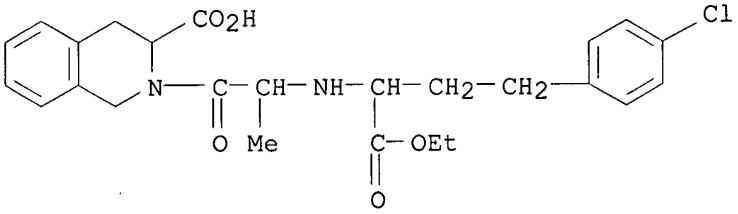
RN 82713-52-8 HCAPLUS

CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-

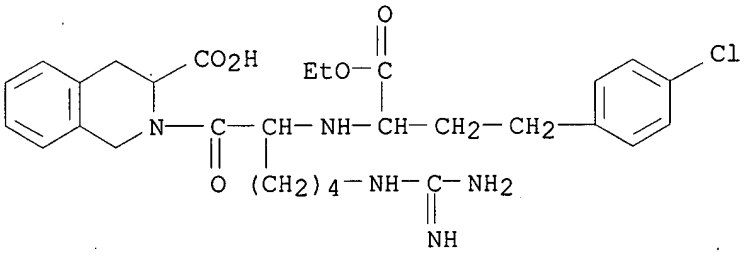
phenylpropyl]amino]-3-hydroxy-1-oxopropyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



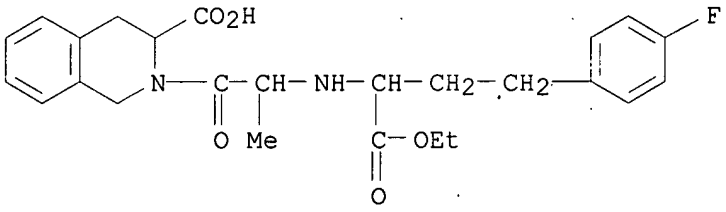
RN 82713-55-1 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[3-(4-chlorophenyl)-1-(ethoxycarbonyl)propyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



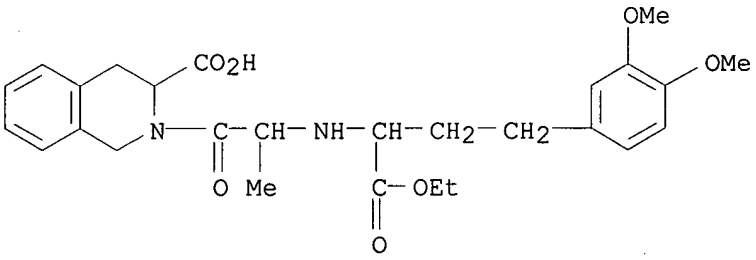
RN 82713-58-4 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[6-[(aminoiminomethyl)amino]-2-[[3-(4-chlorophenyl)-1-(ethoxycarbonyl)propyl]amino]-1-oxohexyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



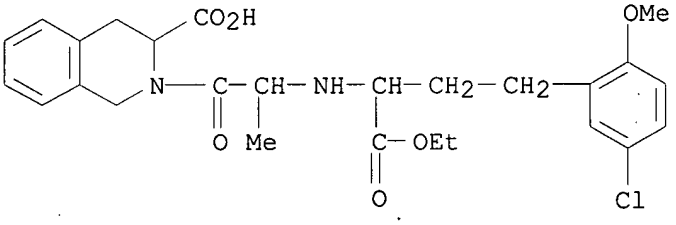
RN 82713-62-0 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-(4-fluorophenyl)propyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



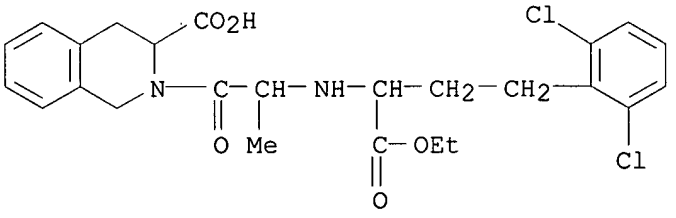
RN 82713-63-1 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[3-(3,4-dimethoxyphenyl)-1-(ethoxycarbonyl)propyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



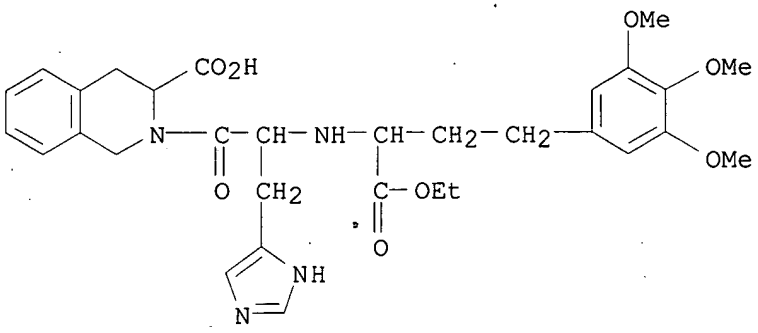
RN 82713-64-2 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[3-(5-chloro-2-methoxyphenyl)-1-(ethoxycarbonyl)propyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



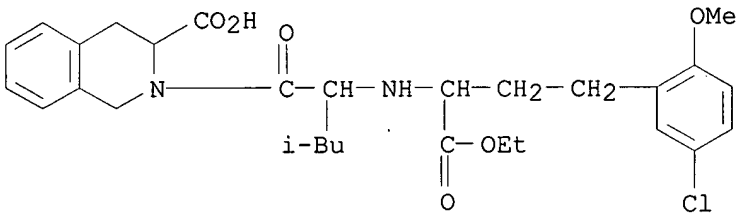
RN 82713-65-3 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[3-(2,6-dichlorophenyl)-1-(ethoxycarbonyl)propyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



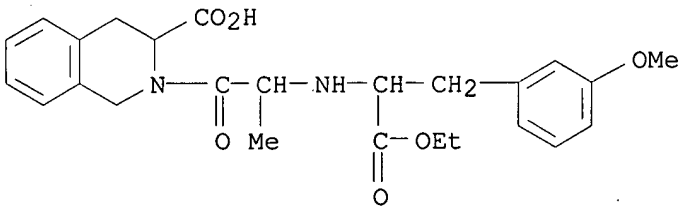
RN 82713-66-4 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-(3,4,5-trimethoxyphenyl)propyl]amino]-3-(1H-imidazol-4-yl)-1-oxopropyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



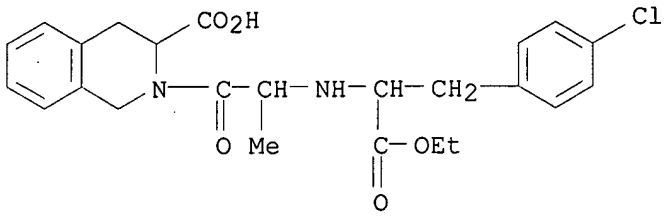
RN 82713-90-4 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[3-(5-chloro-2-methoxyphenyl)-1-(ethoxycarbonyl)propyl]amino]-4-methyl-1-oxopentyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



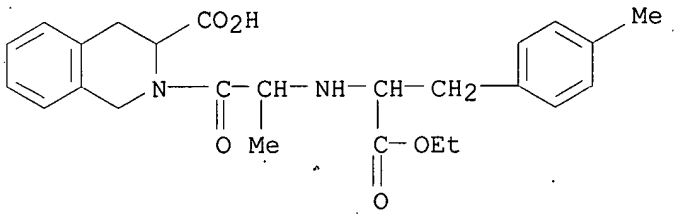
RN 82714-28-1 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[2-ethoxy-1-[(3-methoxyphenyl)methyl]-2-oxoethyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



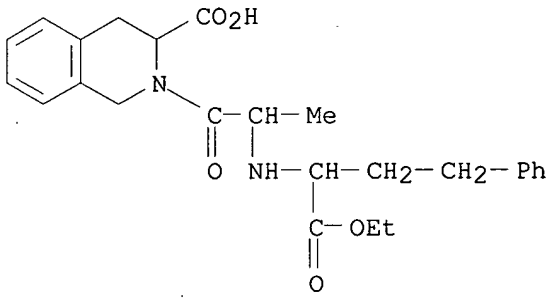
RN 82714-29-2 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-[(4-chlorophenyl)methyl]-2-ethoxy-2-oxoethyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



RN 82714-32-7 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[2-ethoxy-1-[(4-methylphenyl)methyl]-2-oxoethyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



RN 82768-84-1 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)

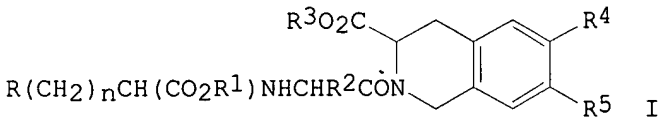


L12 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1982:472257 HCAPLUS
DOCUMENT NUMBER: 97:72257
TITLE: Substituted acyl derivatives of 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acids, their salts and pharmaceutical compositions containing the derivatives or salts
INVENTOR(S): Hoefle, Milton Louis; Klutchko, Sylvester
PATENT ASSIGNEE(S): Warner-Lambert Co. , USA
SOURCE: Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 49605	A1	19820414	EP 1981-304541	19811001
EP 49605	B1	19870318		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4344949	A	19820817	US 1981-236397	19810220
EP 96157	A2	19831221	EP 1983-102092	19811001
EP 96157	A3	19840912		
EP 96157	B1	19870325		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 25974	E	19870415	AT 1981-304541	19811001
AT 26120	E	19870415	AT 1983-102092	19811001
PRIORITY APPLN. INFO.:			US 1980-193767	19801003
			US 1981-236397	19810220
			EP 1981-304541	19811001

GI



I

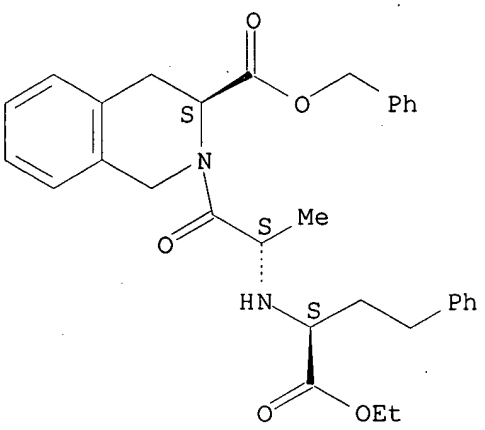
AB Isoquinolinecarboxylates I (R = Ph, substituted Ph; R1 = H, alkyl; R2 = H, alkyl, CH2Ph; R3 = H, alkyl, aralkyl; R4, R5 = H, alkyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, OH; R4R5 = OCH2O; n = 0-3) were prepd. Thus, 6,7-dimethoxy-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid was converted to its benzyl ester and treated with (S,S)-HO2CCHMeNHCH(CO2Et)CH2CH2Ph (II) to give I (R = Ph, R1 = Et, R2 = Me, R3 = CH2Ph, R4 = R5 = OMe, n = 2) which was hydrogenated to I (R = Ph, R1 = Et, R2 = Me, R3 = H, R4 = R5 = OMe, n = 2)(III). II was obtained by treating H-Ala-OCMe3 with PhCH2CH2CHBrCO2Et and hydrolysis. III had an angiotensin converting enzyme-inhibiting ED50 of 5.6 .times. 10-9 M in vitro.

IT **82586-53-6P 82637-57-8P 82637-58-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 82586-53-6 HCAPLUS

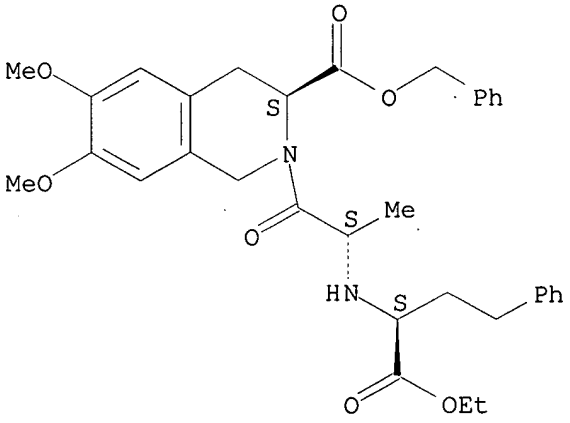
CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, phenylmethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 82637-57-8 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, phenylmethyl ester, [3S-[2[R*(R*)],3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

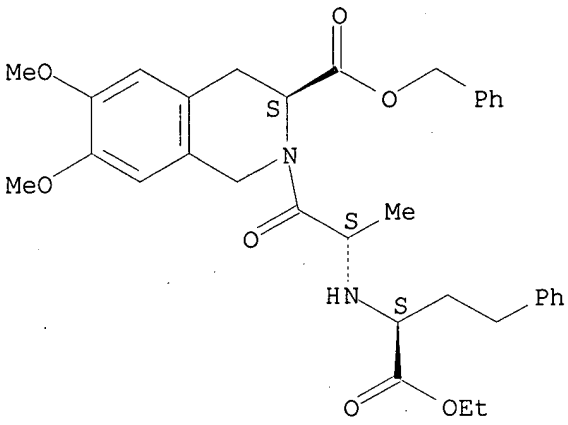


RN 82637-58-9 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, phenylmethyl ester, (3S)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82637-57-8
CMF C34 H40 N2 O7

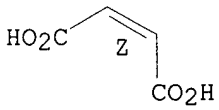
Absolute stereochemistry.



CM 2

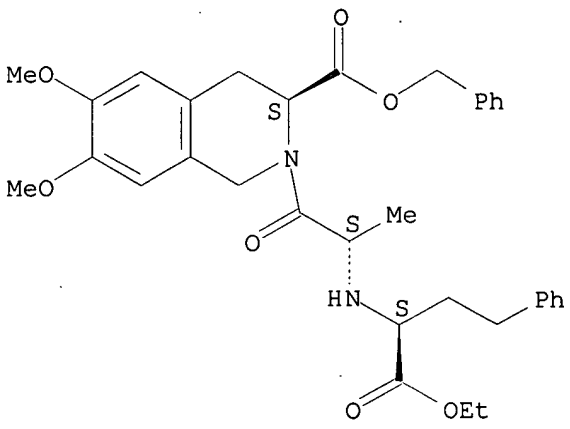
CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



IT **82586-51-4P 82586-54-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn., hydrogenation, and antihypertensive activity of)
RN 82586-51-4 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, phenylmethyl ester, monohydrochloride, [3S-[2[R*(R*)],3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



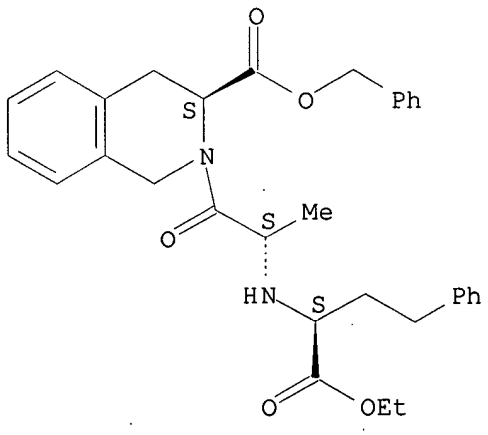
● HCl

RN 82586-54-7 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, phenylmethyl ester, (3S)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82586-53-6
CMF C32 H36 N2 O5

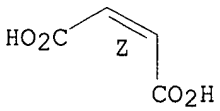
Absolute stereochemistry. Rotation (-).



CM 2

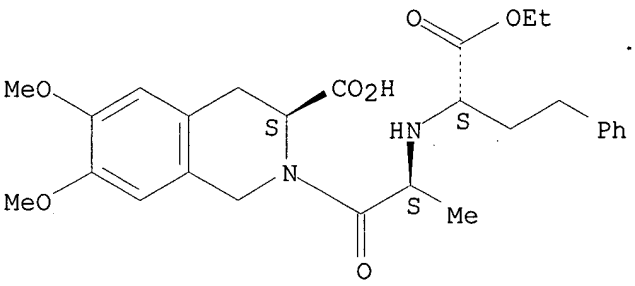
CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



IT **82586-52-5P 82586-55-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn., hydrolysis, and antihypertensive activity of)
RN 82586-52-5 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, monohydrochloride, (3S)- (9CI) (CA INDEX NAME)

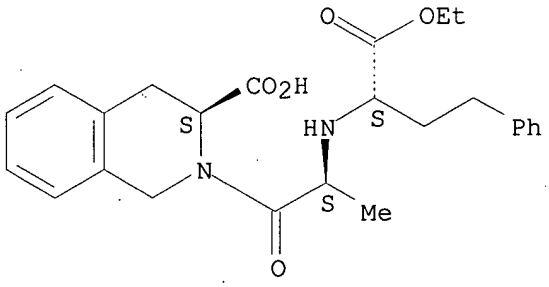
Absolute stereochemistry.



● HCl

RN 82586-55-8 HCAPLUS
CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-, monohydrochloride, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

FILE 'REGISTRY' ENTERED AT 12:03:15 ON 21 APR 2003

L13 38 SEA FILE=REGISTRY ABB=ON PLU=ON (82586-55-8/BI OR 82586-53-6/BI OR 85441-61-8/BI OR 82586-52-5/BI OR 82637-57-8/BI OR 82637-58-9/BI OR 82586-54-7/BI OR 82768-84-1/BI OR 89300-89-0/BI OR 103775-05-9/BI OR 103775-06-0/BI OR 103775-09-3/BI OR 103775-10-6/BI OR 103775-11-7/BI OR 103775-12-8/BI OR 103833-14-3/BI OR 103833-15-4/BI OR 103833-16-5/BI OR 143381-51-5/BI OR 82586-51-4/BI OR 82713-51-7/BI OR 82713-52-8/BI OR 82713-55-1/BI OR 82713-58-4/BI OR 82713-62-0/BI OR 82713-63-1/BI OR 82713-64-2/BI OR 82713-65-3/BI OR 82713-66-4/BI OR 82713-90-4/BI OR 82714-28-1/BI OR 82714-29-2/BI OR 82714-32-7/BI OR 84048-96-4/BI OR 85892-46-2/BI OR 89083-69-2/BI OR 89245-28-3/BI OR 89300-87-8/BI)

FILE 'CAOLD' ENTERED AT 12:03:32 ON 21 APR 2003
L14 0 S L13

FILE 'USPATFULL' ENTERED AT 12:03:40 ON 21 APR 2003
L15 12 S L13/P

L15 ANSWER 1 OF 12 USPATFULL
ACCESSION NUMBER: 1999:137527 USPATFULL
TITLE: Process for preparing N-[1- (S)-ethoxycarbonyl-3-phenylpropyl]-L-alanine derivatives
INVENTOR(S): Yang, Suh-Wan, Tao-yuan Hsien, Taiwan, Province of China
Chang, Yu-An, Tao-yuan Hsien, Taiwan, Province of China
Liu, Yu-Liang, Taipei, Taiwan, Province of China
PATENT ASSIGNEE(S): Everlight USA, Inc., Pineville, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5977380		19991102	
APPLICATION INFO.:	US 1999-251341		19990217	(9)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Powers, Fiona T.
LEGAL REPRESENTATIVE: Bacon & Thomas
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 168
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A process for synthesizing N-[1-(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanine derivatives of the following formula (I): ##STR1## in which the definition of R has the same meaning as given in the description by using a sulfite derivative to activate the C-terminus of the three dimensional structure of an amino acid of N-[1-(S)-ethoxycarbonyl-3- phenylpropyl]-L-alanine, which can effectively couple with another amino acid to form a dipeptide of formula (I). The compound of fomula (I) is an inhibitor of ACE.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 2 OF 12 USPATFULL
ACCESSION NUMBER: 1999:19330 USPATFULL

TITLE: Process for preparing an angiotensin converting enzyme inhibitor
INVENTOR(S): Wang, Shin-Shin, Hsinchu, Taiwan, Province of China
Tsai, Hui-Ping, Changhua, Taiwan, Province of China
PATENT ASSIGNEE(S): Industrial Technology Research Institute, Hsinchu, Taiwan, Province of China (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5869671		19990209
APPLICATION INFO.:	US 1998-106288		19980629

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Barts, Samuel
LEGAL REPRESENTATIVE: Sughrue, Mion, Zinn, Macpeak & Seas, PLLC
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
LINE COUNT: 290
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A process for preparing an angiotensin converting enzyme inhibitor. Phosphorus pentachloride is reacted with the carboxylic acid group of an amino acid to form an acyl chloride hydrochloride. The resulting hydrochloride salt is then coupled with a silylated amino acid in a non-aqueous medium to form a high yield peptide. The peptide is used as an angiotensin converting enzyme (ACE) inhibitor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 3 OF 12 USPATFULL
ACCESSION NUMBER: 95:27333 USPATFULL
TITLE: Aminoacid derivatives, a process for their preparation, agents containing these compounds, and the use thereof
INVENTOR(S): Geiger, Rolf, Frankfurt am Main, Germany, Federal Republic of
Teetz, Volker, Hofheim am Taunus, Germany, Federal Republic of
Urbach, Hansjorg, Kronberg/Taunus, Germany, Federal Republic of
Scholkens, Bernward, Kelkheim, Germany, Federal Republic of
Henning, Rainer, Giessen, Germany, Federal Republic of
PATENT ASSIGNEE(S): Hoechst Aktiengesellschaft, Frankfurt am Main, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5401766		19950328
APPLICATION INFO.:	US 1994-208443		19940309 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1981-297191, filed on 28 Aug 1981, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1980-30327094	19800830
	DE 1981-31181910	19810508

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Lone, Werren B.
LEGAL REPRESENTATIVE: Curtis, Morris & Safford
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
LINE COUNT: 2404
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Aminoacid derivatives of the formula I ##STR1## A , n, R.sup.1, R.sup.2 and R.sup.3 have the meanings given, and salts thereof, a process for their preparation, pharmaceutical preparations based on these compounds, and their use as medicaments.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 4 OF 12 USPATFULL
ACCESSION NUMBER: 92:97073 USPATFULL
TITLE: Octahydroindole-2-carboxylic acids
INVENTOR(S): Geiger, Rolf, Frankfurt am Main, Germany, Federal Republic of
Teetz, Volker, Hofheim am Taunus, Germany, Federal Republic of
Urbach, Hansjorg, Kronberg/Taunus, Germany, Federal Republic of
Scholkens, Bernward, Kelkheim, Germany, Federal Republic of
Henning, Rainer, Giessen, Germany, Federal Republic of
PATENT ASSIGNEE(S): Hoechst Aktiengesellschaft, Frankfurt am Main, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5162362		19921110
APPLICATION INFO.:	US 1983-565887		19831227 (6)

RELATED APPLN. INFO.: Division of Ser. No. US 1981-297191, filed on 28 Aug 1981

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1980-3032709	19800830
	DE 1981-3118191	19810508

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Vaughn, V.
ASSISTANT EXAMINER: Turnipseed, James H.
LEGAL REPRESENTATIVE: Curtis, Morris & Safford
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 1372
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB What are disclosed are aminoacid compounds of the formula ##STR1## wherein n is 0 or 1, and salts thereof, said compounds and salts

having hypotensive properties; methods for making the compounds; pharmaceutical compositions containing the compounds or salts; and use of the compounds and salts for treating hypertension.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 5 OF 12 USPATFULL

ACCESSION NUMBER:	92:89070 USPATFULL
TITLE:	Decahydroisoquinoline carboxylic acids
INVENTOR(S):	Geiger, Rolf, Frankfurt am Main, Germany, Federal Republic of Teetz, Volker, Hofheim am Taunus, Germany, Federal Republic of Urbach, Hansjorg, Kronberg/Taunus, Germany, Federal Republic of Scholkens, Bernward, Kelkheim(Taunus), Germany, Federal Republic of Henning, Rainer, Giessen, Germany, Federal Republic of
PATENT ASSIGNEE(S):	Hoechst Aktiengesellschaft, Frankfurt am Main, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5158959		19921027
APPLICATION INFO.:	US 1983-565900		19831227 (6)
RELATED APPLN. INFO.:	Division of Ser. No. US 1981-297191, filed on 28 Aug 1981		

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1980-3032709	19800830
	DE 1981-3118191	19810508

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Ivy, C. Warren
ASSISTANT EXAMINER:	Turnipseed, James H.
LEGAL REPRESENTATIVE:	Curtis, Morris & Safford
NUMBER OF CLAIMS:	6
EXEMPLARY CLAIM:	1
LINE COUNT:	1525

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB What are disclosed are aminoacid compounds of the formula ##STR1## wherein n is 0 or 1, and salts thereof, said compounds and salts having hypotensive properties; methods for making the compounds; pharmaceutical compositions containing the compounds or salts; and use of the compounds and salts for treating hypertension.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 6 OF 12 USPATFULL

ACCESSION NUMBER:	91:96454 USPATFULL
TITLE:	Process for the preparation of n octahydropenta (6) pyrrole carboxylates
INVENTOR(S):	Teetz, Volker, Hofheim am Taunus, Germany, Federal Republic of Wissmann, Hans, Bad Soden am Taunus, Germany,

Federal Republic of
Urbach, Hansjorg, Kronberg/Taunus, Germany,
Federal Republic of

PATENT ASSIGNEE(S): Hoechst Aktiengesellschaft, Frankfurt am Main, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5068351		19911126
APPLICATION INFO.:	US 1990-560004		19900727 (7)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1989-403919, filed on 7 Sep 1989, now abandoned which is a continuation of Ser. No. US 1988-178767, filed on 30 Mar 1988, now abandoned which is a continuation of Ser. No. US 1986-943882, filed on 19 Dec 1986, now abandoned which is a continuation of Ser. No. US 1984-650715, filed on 14 Sep 1984, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1983-3333454	19830916

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Lee, Lester L.
LEGAL REPRESENTATIVE: Finnegan, Henderson, Farabow, Garrett & Dunner
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
LINE COUNT: 850
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a process for the preparation of compounds of the formula I ##STR1## in which n is 1 or 2, R denotes hydrogen or an organic radical, R.sup.1 denotes an organic radical, R.sup.2 and R.sup.3 are identical or different and denote hydrogen or an organic radical, and R.sup.4 and R.sup.5, together with the atoms bearing them, form a monocyclic, bicyclic or tricyclic heterocyclic ring system having 5 to 15 carbon atoms, which process comprises reacting compounds of the formula II defined in the description with compounds of the formula IV defined in the description, in the presence of phosphinic anhydrides of the formula III, where appropriate eliminating radicals which have been introduced to protect other functional groups and, where appropriate, esterifying free carboxyl groups in a manner known per se.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 7 OF 12 USPATFULL
ACCESSION NUMBER: 91:82338 USPATFULL
TITLE: Process for the preparation of octahydropenta(b)pyrrole carboxylates
INVENTOR(S): Urbach, Hansjorg, Kronberg/Taunus, Germany, Federal Republic of
Henning, Rainer, Hattersheim am Main, Germany, Federal Republic of
Wissmann, Hans, Bad Soden am Taunus, Germany, Federal Republic of
Teetz, Volker, Hofheim am Taunus, Germany,

	Federal Republic of
PATENT ASSIGNEE(S):	Hoechst Aktiengesellschaft, Frankfurt am Main, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5055591		19911008
APPLICATION INFO.:	US 1988-173024		19880323 (7)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1986-943881, filed on 19 Dec 1986, now abandoned which is a continuation of Ser. No. US 1984-650714, filed on 14 Sep 1984, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1983-3333455	19830916

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Lee, Lester L.
LEGAL REPRESENTATIVE: Finnegan, Henderson, Farabow, Garrett, and Dunner
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
LINE COUNT: 855
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a process for the preparation of compounds of the formula I ##STR1## in which n is 1 or 2, R denotes hydrogen or an organic radical, R.sup.1 denotes an organic radical, R.sup.2 and R.sup.3 are identical or different and denote hydrogen or an organic radical, and R.sup.4 and R.sup.5, together with the atoms bearing them, form a monocyclic, bicyclic or tricyclic heterocyclic ring system having 3 to 15 carbon atoms, which process comprises reacting compounds of the formula II defined in the description with compounds of the formula III defined in the description, in the presence of alkanephosphonic anhydrides, where appropriate eliminating radicals which have been introduced to protect other functional groups and, where appropriate, esterifying free carboxyl groups in a manner known per se.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 8 OF 12 USPATFULL
ACCESSION NUMBER: 88:48826 USPATFULL
TITLE: Crystalline quinapril and a process for producing the same
INVENTOR(S): Goel, Om P., Ann Arbor, MI, United States
Krolls, Uldis, Ann Arbor, MI, United States
PATENT ASSIGNEE(S): Warner-Lambert Company, Morris Plains, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4761479		19880802
APPLICATION INFO.:	US 1987-32209		19870330 (7)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Hollrah, Glennon H.

ASSISTANT EXAMINER: Turnipseed, James H.
LEGAL REPRESENTATIVE: Anderson, Elizabeth M.
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 237
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A novel crystalline form of quinapril and a novel process for the large scale preparation of the ACE inhibitor, quinapril, in a highly pure state. The substance is of high bulk density suitable for formulation in capsules and tablets. This inexpensive process uses HCl gas in glacial acetic acid for rapid and clean de-t-butylation at room temperature.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 9 OF 12 USPATFULL
ACCESSION NUMBER: 85:44762 USPATFULL
TITLE: N-substituted amino acids as intermediates in the preparation of acyl derivatives of 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acids
INVENTOR(S): Hoefle, Milton L., Ann Arbor, MI, United States
Klutchko, Sylvestor, Ann Arbor, MI, United States
PATENT ASSIGNEE(S): Warner-Lambert Company, Morris Plains, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4532342		19850730
APPLICATION INFO.:	US 1982-386375		19820608 (6)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1981-236397, filed on 20 Feb 1981, now patented, Pat. No. US 4344949 which is a continuation-in-part of Ser. No. US 1980-193767, filed on 3 Oct 1980, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Hollrah, Glennon H.
ASSISTANT EXAMINER: Turnipseed, James H.
LEGAL REPRESENTATIVE: Daignault, Ronald A.
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1
LINE COUNT: 555
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB N-substituted amino acids are described which when coupled with 1,2,3,4-tetrahydroisoquinolines result in substituted acyl derivatives of 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acids as anti-hypertensive agents. The novel intermediates are in turn prepared by reacting an amino acid such as alanine with 2-bromo-4-phenyl butanoic acid or an ester thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 10 OF 12 USPATFULL
ACCESSION NUMBER: 84:8849 USPATFULL
TITLE: Antihypertensive agents
INVENTOR(S): Smith, Elizabeth M., Verona, NJ, United States
Witkowski, Joseph T., Morris Township, Morris County, NJ, United States

PATENT ASSIGNEE(S): Schering Corporation, Kenilworth, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4431645		19840214	
APPLICATION INFO.:	US 1982-355639		19820308	(6)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Ford, John M.
LEGAL REPRESENTATIVE: Magatti, Anita W., Eisen, Bruce M.
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1,16
LINE COUNT: 444
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds of the formula ##STR1## and the pharmaceutically acceptable salts thereof, wherein R.sup.1, R.sup.2, R.sup.3 and R.sup.4 are independently selected from hydrogen or lower alkyl; n is 1 or 0; A and B taken together with the carbons to which they are attached form an alkylene ring having six carbon atoms or A and B are hydrogen; and Z is ##STR2## The compounds are useful as hypertensive agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 11 OF 12 USPATFULL
ACCESSION NUMBER: 84:8848 USPATFULL
TITLE: Antihypertensive agents
INVENTOR(S): Smith, Elizabeth M., Verona, NJ, United States
Witkowski, Joseph T., Morris Township, Morris County, NJ, United States
Doll, Ronald J., Maplewood, NJ, United States
PATENT ASSIGNEE(S): Schering Corporation, Kenilworth, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4431644		19840214	
APPLICATION INFO.:	US 1982-355638		19820308	(6)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Ford, John M.
LEGAL REPRESENTATIVE: Magatti, Anita W., Eisen, Bruce M.
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1,11
LINE COUNT: 497
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds of the formula ##STR1## and the pharmaceutically acceptable salts thereof, wherein R.sup.1, R.sup.2 and R.sup.4 are independently selected from hydrogen and lower alkyl; R.sup.3 is hydrogen, lower alkyl or amino lower alkyl; A and B taken together with the carbons to which they are attached form an alkylene ring having six carbon atoms or A and B are hydrogen; and Z is ##STR2## are disclosed. The compounds are useful as anti-hypertensive agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 12 OF 12 USPATFULL

ACCESSION NUMBER:	82:39913 USPATFULL
TITLE:	Substituted acyl derivatives of 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acids
INVENTOR(S):	Hoefle, Milton L., Ann Arbor, MI, United States Klutchko, Sylvester, Ann Arbor, MI, United States
PATENT ASSIGNEE(S):	Warner-Lambert Company, Morris Plains, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4344949		19820817
APPLICATION INFO.:	US 1981-236397		19810220 (6)

RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1980-193767, filed on 3 Oct 1980, now abandoned
DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Daus, Donald G.
ASSISTANT EXAMINER:	Turnipseed, James H.
LEGAL REPRESENTATIVE:	Patton, Walter
NUMBER OF CLAIMS:	15
EXEMPLARY CLAIM:	1,15
LINE COUNT:	606

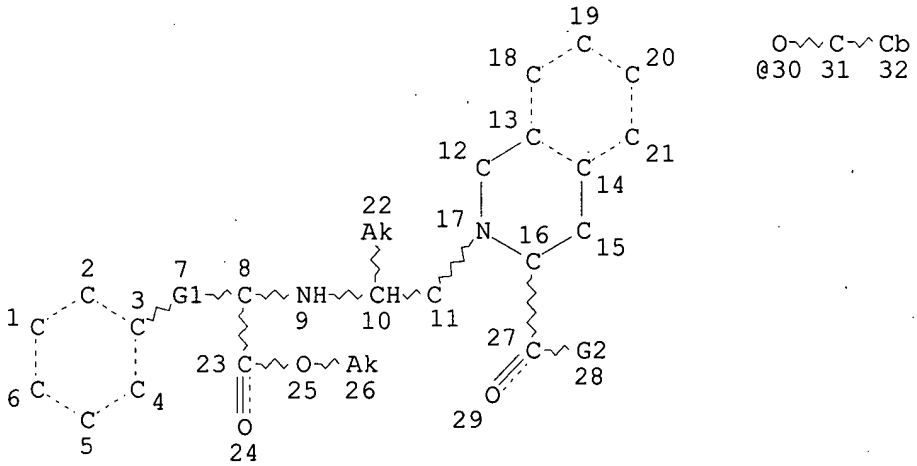
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Substituted acyl derivatives of 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acids and the pharmaceutically acceptable salts thereof are produced by coupling a suitably substituted 1,2,3,4-tetrahydroisoquinoline with a suitably substituted amino acid and when desired hydrolyzing or removing protecting groups of the resulting product. The compounds of the invention, their salts and pharmaceutical compositions thereof are useful as antihypertensive agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

(FILE 'MARPAT' ENTERED AT 12:04:06 ON 21 APR 2003)

L16 STR



REP G1=(1-3) CH2
VAR G2=OH/30

Searcher : Shears 308-4994

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 22 26 32
GGCAT IS UNS AT 32
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L18 17 SEA FILE=MARPAT SSS FUL L16 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 2950 ITERATIONS 17 ANSWERS
SEARCH TIME: 00.00.20

L18 ANSWER 1 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 134:157567 MARPAT
TITLE: Method of using angiotensin converting enzyme inhibitors to stimulate angiogenesis
INVENTOR(S): Isner, Jeffrey Michael
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: U.S., 21 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6191144	B1	20010220	US 1999-361351	19990726
PRIORITY APPLN. INFO.:			US 1998-96814P	19980817

AB The invention is directed to the use of a group of ACE inhibitors to stimulate angiogenesis in mammals or in mammalian tissue in vitro. Specifically, the invention is directed to inducing or enhancing angiogenesis through the administration of a group of ACE inhibitors and to ACE inhibitor-contg. compns. for effecting the inducement or enhancement of angiogenesis. The ACE inhibitors may also be useful in the promotion of angiogenesis, e.g. in the promotion of wound healing, bone healing, and in the treatment of burns, as well as in promoting the formation, maintenance, and repair of tissue. In a preferred embodiment, the ACE inhibitor, quinapril, or quinaprilat, is used to treat, prophylactically or otherwise, mammals in need of angiogenic-treatment.
IC ICM A61K031-445
NCL 514315000
CC 1-8 (Pharmacology)
Section cross-reference(s): 63
ST angiotensin converting enzyme inhibitor angiogenesis stimulation; ACE inhibitor angiogenesis stimulation wound healing; bone healing ACE inhibitor angiogenesis stimulation; burn ACE inhibitor angiogenesis stimulation; quinapril quinaprilat angiogenesis

stimulation
IT Angiogenesis
Burn
Drug delivery systems
Wound healing promoters
(ACE inhibitors for stimulation of angiogenesis)
IT Blood vessel
(collateral; ACE inhibitors for stimulation of angiogenesis)
IT Bone
(healing; ACE inhibitors for stimulation of angiogenesis)
IT Transplant and Transplantation
(skin; ACE inhibitors for stimulation of angiogenesis)
IT Skin
(transplant; ACE inhibitors for stimulation of angiogenesis)
IT 62571-86-2, Captopril 127464-60-2, Vascular endothelial growth factor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(ACE inhibitors for stimulation of angiogenesis)
IT 82768-85-2, Quinaprilat 85441-61-8, Quinapril
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ACE inhibitors for stimulation of angiogenesis)
IT 9015-82-1, Angiotensin converting enzyme
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ACE inhibitors for stimulation of angiogenesis)
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 132:15667 MARPAT
TITLE: Stabilization of formulations containing ACE inhibitors by magnesium oxide
INVENTOR(S): Daniel, Jane Ellen; Harris, Michael Ray; Hokanson, Gerard Clifford; Weiss, Jay
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9962560	A1	19991209	WO 1999-US10189	19990510
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2330581	AA	19991209	CA 1999-2330581	19990510
AU 9939793	A1	19991220	AU 1999-39793	19990510

BR 9910947	A	20010306	BR 1999-10947	19990510
EP 1083931	A1	20010321	EP 1999-922899	19990510
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002516881	T2	20020611	JP 2000-551814	19990510
NZ 508544	A	20021025	NZ 1999-508544	19990510
US 6417196	B1	20020709	US 2000-700883	20001120
NO 2000006148	A	20001204	NO 2000-6148	20001204
US 2002161020	A1	20021031	US 2002-127181	20020422
PRIORITY APPLN. INFO.:			US 1998-88280P	19980605
			WO 1999-US10189	19990510
			US 2000-700883	20001120

AB The present invention is directed to ACE inhibitor-contg. compns. stabilized by the presence of magnesium oxide. Preferably, the ACE inhibitor, quinapril, is protected from certain forms of degrdn. when prepd. in a pharmaceutical compn. consisting essentially of magnesium oxide as the stabilizing agent. The presence of magnesium oxide also lends itself to favorable processing conditions during the manuf. of ACE inhibitor-contg. compns., esp. processing by wet granulation. Thus, tablets contained quinapril-HCl 21.7, MgO 21.7, lactose 254.3, gelatin 6.4, Polyplasdone 12.8, and Mg stearate 3.2 mg. The MgO-contg. formulation required less gelatin than the Mg carbonate hydroxide formulation to obtain acceptable compressibility and stabilized the formulation.

IC ICM A61K047-02
ICS A61K047-26; A61K031-47

CC 63-6 (Pharmaceuticals)

ST stabilization formulation ACE inhibitor magnesium oxide

IT Friction
Stabilizing agents
(stabilization of formulations contg. ACE inhibitors by magnesium oxide)

IT Drug delivery systems
(tablets; stabilization of formulations contg. ACE inhibitors by magnesium oxide)

IT Granulation
(wet; stabilization of formulations contg. ACE inhibitors by magnesium oxide)

IT 9015-82-1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; stabilization of formulations contg. ACE inhibitors by magnesium oxide)

IT 82586-55-8, Quinapril hydrochloride 85441-61-8, Quinapril
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilization of formulations contg. ACE inhibitors by magnesium oxide)

IT 63-42-3, Lactose 69-65-8, Mannitol 1309-48-4, Magnesium oxide (MgO), biological studies 75847-73-3, Enalapril 80876-01-3, Indolapril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilization of formulations contg. ACE inhibitors by magnesium oxide)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 17 MARPAT COPYRIGHT 2003 ACS

ACCESSION NUMBER: 131:322920 MARPAT
TITLE: Process for preparing N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanine derivatives
INVENTOR(S): Yang, Suh-Wan; Chang, Yu-An; Liu, Yu-Liang
PATENT ASSIGNEE(S): Everlight USA, Inc., USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5977380	A	19991102	US 1999-251341	19990217

PRIORITY APPLN. INFO.: US 1999-251341 19990217
OTHER SOURCE(S): CASREACT 131:322920
AB (S)-EtO2CCH(CH2CH2Ph)-Ala-R (I; R are certain cyclic amino acids, e.g., L-proline) or their pharmaceutically acceptable salts were prepd. by coupling I (R = OC6H4R1, where R1 is nitro, cyano, sulfite, carboxy, aldehyde, ester, or halo) with an amino acid. Thus, I (R = OC6H4NO2-p), formed by esterifying the acid with 4-nitrophenol in the presence of triethylamine and thionyl chloride in dichloromethane, was treated with L-proline to afford I (R = proline residue) (enalapril).
IC ICM C07D207-12
ICS C07D233-26; C07D217-16; C07D495-10
NCL 548533000
CC 34-3 (Amino Acids, Peptides, and Proteins)
ST ethoxycarbonylphenylpropylalanyl dipeptide prepn; peptide ethoxycarbonylphenylpropylalanyl prepn; enalapril prepn
IT Dipeptides
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of [(ethoxycarbonyl)phenylpropyl]-L-alanine derivs.)
IT 75847-73-3P, Enalapril 76095-16-4P, Enalapril maleate 80876-01-3P 83059-56-7P 83435-66-9P 83647-97-6P 85441-61-8P 87333-19-5P 89371-37-9P 103775-10-6P 109683-61-6P
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of [(ethoxycarbonyl)phenylpropyl]-L-alanine derivs.)
IT 147-85-3, L-Proline, reactions 25887-81-4 74163-81-8 80871-70-1 80875-98-5 82717-96-2 83552-44-7 103733-66-0 107716-98-3 109428-53-7 109583-12-2 248254-17-3 248254-18-4 248254-19-5 248606-38-4 248606-39-5 248606-40-8 248606-41-9 248606-42-0 248606-43-1 248606-44-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of [(ethoxycarbonyl)phenylpropyl]-L-alanine derivs.)
IT 248254-21-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of [(ethoxycarbonyl)phenylpropyl]-L-alanine derivs.)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:168658 MARPAT

TITLE: Process for preparing pharmacologically acceptable salts of N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanyl amino acids

INVENTOR(S): Ueda, Yasuyoshi; Kinoshita, Koichi; Moroshima, Tadashi; Yanagida, Yoshifumi; Fuse, Yoshihide

PATENT ASSIGNEE(S): Kaneka Corporation, Japan

SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

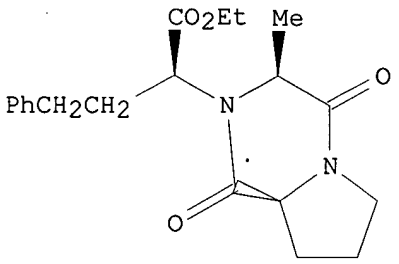
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9905164	A1	19990204	WO 1998-JP3240	19980721
W: CA, CN, HU, IL, JP, KR, SG, SI, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 967221	A1	19991229	EP 1998-932585	19980721
R: AT, CH, DE, ES, FR, GB, IT, LI, NL, IE				
US 6335453	B1	20020101	US 1999-269107	19990319
US 2002087007	A1	20020704	US 2001-989186	20011121
US 6518436	B2	20030211		
PRIORITY APPLN. INFO.:			JP 1997-195865	19970722
			WO 1998-JP3240	19980721

OTHER SOURCE(S): CASREACT 130:168658

GI



II

AB Claimed is a process for prepg. pharmacol. acceptable salts of N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanyl amino acids, comprising the steps of: condensing an amino acid with N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanine N-carboxy anhydride (I) under basic conditions; decarboxylating the condensate under neutral to acidic conditions to prep. an N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanyl amino acid; and converting the product to a pharmacol. acceptable salt thereof, characterized in that a series of procedures up to the formation of a pharmacol. acceptable salt or up to the withdrawal of the pharmaceutically acceptable salt thereof are carried out in an aq. liq. to inhibit the prodn. of a byproduct diketopiperazine, e.g. II. According to this process, high-quality pharmacol. acceptable salts of N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanyl amino acids can be prepd. in high yields in a cost-effective manner on a com. scale. Thus, a soln. of 29.20 g I in 156 mL EtOAc was slowly added dropwise over 4 h at 19-20.degree.

to a mixt. of 22.02 g L-proline, 20 mL EtOAc, and 22 mL H2O (adjusted to pH 10.5 by adding 30 wt.% aq. NaOH) with stirring, while the pH of the reaction mixt. was kept at pH 10.5.+-.0.5 by adding 30 wt.% aq. NaOH during the reaction. After completing the addn., the reaction mixt. was stirred for another 1 h under the same condition, warmed to 30.degree., made pH 4.5.+-.0.2 by adding 35% wt.% aq. HCl, and stirred for 10 min to complete decarboxylation. The org. phase was sepd. and the aq. phase was extd. once with EtOAc. The ext. was combined and washed once with 5% vol. of H2O to give the water-satd. org. phase contg. N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanyl-L-proline (enalapril) (III) 14, II 0.5, N-[1(S)-carboxy-3-phenylpropyl]-L-alanyl-L-proline 0.4, and N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanine 0.5 wt.%. To the org. phase was added 10.49 g maleic acid and the resulting mixt. was stirred at 30.degree. for 1 h, cooled to 3.degree. over 3 h, and was stirred for another 2 h to give, after filtration of the pptd. crystals, washing them with EtOAc chilled to 5.degree., and vacuum drying, 90% III maleate of .gtoreq.99% purity.

IC ICM C07K005-062
ICS C07K001-02; C07K001-08

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

ST ethoxycarbonylphenylpropylalanyl amino acid prepn enalapril; ethoxycarbonylphenylpropylalanine carboxy anhydride condensation amino acid

IT Dipeptides
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pharmacol. acceptable salts of N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanyl amino acids)

IT 76420-72-9P 82717-96-2P 115729-52-7P
RL: BYP (Byproduct); REM (Removal or disposal); PREP (Preparation); PROC (Process)
(prepn. of pharmacol. acceptable salts of N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanyl amino acids)

IT 147-85-3, L-Proline, reactions 67123-97-1, 1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid 84793-24-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of pharmacol. acceptable salts of N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanyl amino acids)

IT 220069-65-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of pharmacol. acceptable salts of N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanyl amino acids)

IT 75847-73-3P, Enalapril 76095-16-4P, Enalapril maleate
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pharmacol. acceptable salts of N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanyl amino acids)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:139658 MARPAT
TITLE: Process for preparing enalapril and related angiotensin converting enzyme inhibitors
INVENTOR(S): Wang, Shin-Shin; Tsai, Hui-Ping

PATENT ASSIGNEE(S): Industrial Technology Research Institute, Taiwan
SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5869671	A	19990209	US 1998-106288	19980629

PRIORITY APPLN. INFO.: US 1998-106288 19980629
OTHER SOURCE(S): CASREACT 130:139658

AB Amino acid derivs. R1R2CHCOA (R1 = R3O2CCHR4NH or AcSCH2; R2 = alkyl; R3 = alkyl, Ph, phenylmethyl; R4 = phenylalkyl, Ph, alkyl; A = an amino acid residue) were prepd. as angiotensin converting enzyme inhibitors. Thus, treating N-[1-(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanine with PCl5 and coupling of the acyl chloride with L-proline in the presence of hexamethyldisilazane afforded 79.4% enalapril.

IC ICM C07D217-00
NCL 546147000
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7
ST enalapril prepn process; quinapril prepn process; peptide prepn inhibitor angiotensin converting enzyme
IT Peptides, preparation
RL: IMF (Industrial manufacture); PREP (Preparation)
(process for prepg. enalapril and related angiotensin converting enzyme inhibitors)
IT 10416-59-8, BSA
RL: RCT (Reactant); RACT (Reactant or reagent)
(bis(trimethylsilyl)acetamide; process for prepg. enalapril and related angiotensin converting enzyme inhibitors)
IT 9015-82-1, Angiotensin converting enzyme
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(process for prepg. enalapril and related angiotensin converting enzyme inhibitors)
IT 64838-55-7P 75847-73-3P, Enalapril 85441-61-8P, Quinapril
RL: IMF (Industrial manufacture); PREP (Preparation)
(process for prepg. enalapril and related angiotensin converting enzyme inhibitors)
IT 999-97-3, Hmds 74163-81-8 82717-96-2 148493-16-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for prepg. enalapril and related angiotensin converting enzyme inhibitors)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 129:28219 MARPAT
TITLE: Preparation of organic nitrates as antithrombotics.
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.; Del Soldato, Piero
SOURCE: PCT Int. Appl., 42 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9821193	A1	19980522	WO 1997-EP6311	19971112
W: AL, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9855519	A1	19980603	AU 1998-55519	19971112
AU 729423	B2	20010201		
EP 941218	A1	19990915	EP 1997-951890	19971112
EP 941218	B1	20021016		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, SI, LT, FI, RO				
CN 1242768	A	20000126	CN 1997-181245	19971112
CN 1094931	B	20021127		
BR 9712959	A	20000201	BR 1997-12959	19971112
JP 2001507676	T2	20010612	JP 1998-522179	19971112
RU 2190594	C2	20021010	RU 1999-112517	19971112
AT 226199	E	20021115	AT 1997-951890	19971112
US 6242432	B1	20010605	US 1999-297933	19990511
KR 2000053251	A	20000825	KR 1999-704229	19990512
PRIORITY APPLN. INFO.:			IT 1996-MI2368	19961114
			WO 1997-EP6311	19971112

AB A(XNO2)t (t = 1, 2; X = alkylene; A = specified residue of cardiovascular agent, preferably timolol or enalapril), were prepd. Thus, enalapril was N-BOC protected followed by condensation with 3-HOC6H4CH2ONO2 in the presence of DCC and deprotection with HCl in EtOAc to give enalapril 3-(nitroxymethyl)phenyl ester. The latter at 10 mg/kg orally in rats gave 53% antithrombotic activity, vs. 11% for enalapril.

IC ICM C07D285-10
ICS C07K005-062; A61K031-41; A61K038-05

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 28

ST org nitrate prepn antithrombotic; timolol nitrate deriv prepn antithrombotic; enalapril nitrate deriv prepn antithrombotic; antihypertensive org nitrate prepn; platelet aggregation inhibitor org nitrate

IT Anticoagulants
Antihypertensives
Bronchodilators
Platelet aggregation inhibitors
(prepn. of org. nitrates as antithrombotics)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of org. nitrates as antithrombotics)

IT 207987-07-3P 207987-09-5P 207987-11-9P 207987-13-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of org. nitrates as antithrombotics)
IT 927-58-2, 4-Bromobutyryl chloride 26839-77-0 75847-73-3, Enalapril 76420-72-9 190442-16-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of org. nitrates as antithrombotics)
IT 26839-76-9P, R-Timolol 207987-15-3P 207987-17-5P 207987-19-7P 207987-21-1P 207987-23-3P 207987-25-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of org. nitrates as antithrombotics)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 128:61791 MARPAT
TITLE: Method for the production of L-alanine derivatives with an ACE inhibitor effect
INVENTOR(S): Palomo Coll, Alberto; Serra Mortes, Sonia
PATENT ASSIGNEE(S): KRKA Tovarna Zdravil D. D., Slovenia
SOURCE: Ger. Offen., 6 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19721290	A1	19971211	DE 1997-19721290	19970521
PRIORITY APPLN. INFO.:			SI 1996-169	19960522

AB Title compds. R1CH2CH2CH(CO2Et)NHCH(CH3)COR2 [(I): R1 = alkyl, aryl, heterocycle; R2 = (un)natural .alpha.-amino acid],and their pharmaceutically acceptable salts were prepd. as ACE-inhibitors (no data). Thus, (S,S)-I (R1 = Ph; R2 = OH) was reacted with L-proline to yield (S,S)-I (R1 = Ph; R2 = L-proline), which was converted to its maleate salt.
IC C07K005-078; C07D285-12; C07D521-00; C07D207-16; C07D217-26; C07D233-32; C07D209-42; C07D495-10; C07D209-52
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
ST amino acid prepn ACE inhibitor; antihypertensive amino acid prepn; alanine proline prepn ACE inhibitor
IT Antihypertensives
(prepn. of L-alanine derivs. with an ACE inhibitor effect)
IT Amino acids, preparation
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of L-alanine derivs. with an ACE inhibitor effect)
IT 76420-75-2P 87679-37-6P 200423-23-0P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(prepn. of L-alanine derivs. with an ACE inhibitor effect)
IT 75847-73-3P 80876-01-3P 83059-56-7P 83435-66-9P 83647-97-6P
85441-61-8P 87333-19-5P 89371-37-9P 103775-10-6P
109683-61-6P
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of L-alanine derivs. with an ACE inhibitor effect)
IT 147-85-3, L-Proline, reactions 80875-98-5 82717-96-2
145438-94-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of L-alanine derivs. with an ACE inhibitor effect)
IT 200423-22-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of L-alanine derivs. with an ACE inhibitor effect)

L18 ANSWER 8 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 128:35025 MARPAT
TITLE: Process for the preparation of N-(1-alkoxycarbonyl-3-phenylpropyl)amino acid derivatives
INVENTOR(S): Ueda, Yasuyoshi; Matsumoto, Akira; Manabe, Hajime
PATENT ASSIGNEE(S): Kaneka Corporation, Japan; Ueda, Yasuyoshi; Matsumoto, Akira; Manabe, Hajime
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9743246	A1	19971120	WO 1997-JP1543	19970508
W: CA, CN, HU, KR, SG, SI, US				
RW: BE, CH, DE, ES, FR, GB, IE, IT, NL				
JP 09301938	A2	19971125	JP 1996-116545	19960510
CA 2254972	AA	19971120	CA 1997-2254972	19970508
EP 903337	A1	19990324	EP 1997-918383	19970508
R: BE, CH, DE, ES, FR, GB, IT, LI, NL, IE				
CN 1218454	A	19990602	CN 1997-194529	19970508
KR 2000010840	A	20000225	KR 1998-708981	19981106
US 6118010	A	20000912	US 1998-147255	19981110
PRIORITY APPLN. INFO.:			JP 1996-116545	19960510
			WO 1997-JP1543	19970508

OTHER SOURCE(S): CASREACT 128:35025
AB A simple, efficient and high-productivity process for prepg. high-quality N-(1-alkoxycarbonyl-3-phenylpropyl)amino acid derivs. of formula PhCH2CH2CH(CO2R)-X-Y (R = alkyl; X = Ala, Gly, Leu, Ile, Val, Orn or Lys or Hly with .omega.-amino group being protected with acyl-type protecting group; Y = OH, Ala, Gly, Leu, Ile, Val, Pro, Q, Q1, Q2, etc.) contg. few impurities comprises catalytic redn. of N-(1-alkoxycarbonyl-3-oxo-3-phenylpropyl)amino acid derivs. of formula PhCOCH2CH(CO2R)-X-Y (R, X, Y = same as above) in the presence of .gtoreq.3 equiv strong acid per 1 equiv of the 1-alkoxycarbonyl-3-oxo-3-phenylpropyl deriv. in an alc. or a solvent

contg. an alc. with the strong acid concn. of 0.4-5N. This process suppresses the formation of side products, i.e. 1-alkoxycarbonyl-3-cyclohexylpropyl derivs. Thus, 10.0 g N-[(1RS)-1-ethoxycarbonyl-3-oxo-3-phenylpropyl]-L-alanine was added to an aq. EtOH (105 mL) contg. 1.9N H2SO4 and 7 wt.% H2O, followed by adding 5% Pd-C contg. 50 wt.% H2O, and the resulting mixt. was hydrogenated under normal pressure H at 20.degree. and stirring intensity 0.5-1 KW/m3. When H was absorbed at >90% of the required quantity, the feeding of H was stopped and the reaction mixt. was worked up to give 75% N-[(1S)-1-ethoxycarbonyl-3-phenylpropyl]-L-alanine of 99.3 wt.% purity contg. 0.1 wt.% N-(1-ethoxycarbonyl-3-cyclohexylpropyl)-L-alanine and <0.1 wt.% N-(1-carboxy-3-phenylpropyl)-L-alanine.

IC ICM C07C229-36
ICS C07C227-16; C07K005-062; C07K005-068; C07K005-078; C07K001-113

CC 34-3 (Amino Acids, Peptides, and Proteins)

ST alkoxycarbonylphenylpropyl amino acid prepn; alkoxycarbonyloxophenylpropyl amino acid catalytic hydrogenation

IT Hydrogenation catalysts
(palladium; prepn. of N-(1-alkoxycarbonyl-3-phenylpropyl)amino acid derivs. by catalytic hydrogenation of N-(1-alkoxycarbonyl-3-oxo-3-phenylpropyl)amino acid derivs.)

IT Hydrogenation
(prepn. of N-(1-alkoxycarbonyl-3-phenylpropyl)amino acid derivs. by catalytic hydrogenation of N-(1-alkoxycarbonyl-3-oxo-3-phenylpropyl)amino acid derivs.)

IT 84324-12-9P, N-[(R)-1-Ethoxycarbonyl-3-phenylpropyl]-L-alanine 199001-95-1P, N-(1-Ethoxycarbonyl-3-cyclohexylpropyl)-L-alanine 199001-96-2P, N-(1-Carboxy-3-phenylpropyl)-L-alanine 199001-97-3P, N2-(1-Carboxy-3-phenylpropyl)-N6-trifluoroacetyl-L-lysine 199001-99-5P, N2-(1-Ethoxycarbonyl-3-cyclohexylpropyl)-N6-trifluoroacetyl-L-lysine 199002-00-1P, N2-(1-Ethoxycarbonyl-3-cyclohexylpropyl)-N6-trifluoroacetyl-L-lysyl-L-proline 199002-01-2P, N2-(1-Carboxy-3-phenylpropyl)-N6-trifluoroacetyl-L-lysyl-L-proline
RL: BYP (Byproduct); PREP (Preparation)
(prepn. of N-(1-alkoxycarbonyl-3-phenylpropyl)amino acid derivs. by catalytic hydrogenation of N-(1-alkoxycarbonyl-3-oxo-3-phenylpropyl)amino acid derivs.)

IT 7440-05-3, Palladium, uses
RL: CAT (Catalyst use); USES (Uses)
(prepn. of N-(1-alkoxycarbonyl-3-phenylpropyl)amino acid derivs. by catalytic hydrogenation of N-(1-alkoxycarbonyl-3-oxo-3-phenylpropyl)amino acid derivs.)

IT 10009-20-8, N.omega.-Trifluoroacetyl-L-lysine 15121-89-8, Ethyl trans-.beta.-benzoylacrylate 199002-03-4, N-(1-Ethoxycarbonyl-3-oxo-3-phenylpropyl)-L-alanine 199002-04-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of N-(1-alkoxycarbonyl-3-phenylpropyl)amino acid derivs. by catalytic hydrogenation of N-(1-alkoxycarbonyl-3-oxo-3-phenylpropyl)amino acid derivs.)

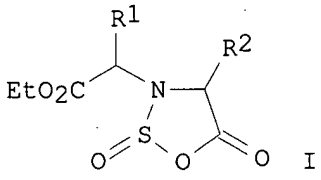
IT 199002-02-3P, N2-(1-Ethoxycarbonyl-3-oxo-3-phenylpropyl)-N6-trifluoroacetyl-L-lysine 199611-78-4P, N2-(1-Ethoxycarbonyl-3-phenylpropyl)-N6-trifluoroacetyl-L-lysyl-L-proline
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of N-(1-alkoxycarbonyl-3-phenylpropyl)amino acid derivs. by catalytic hydrogenation of N-(1-alkoxycarbonyl-3-oxo-3-phenylpropyl)amino acid derivs.)

IT 76547-98-3P, N2-[(S)-1-Carboxy-3-phenylpropyl]-L-lysyl-L-proline
82717-96-2P 199001-98-4P, N2-(1-Ethoxycarbonyl-3-phenylpropyl)-N6-trifluoroacetyl-L-lysine
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of N-(1-alkoxycarbonyl-3-phenylpropyl)amino acid derivs. by catalytic hydrogenation of N-(1-alkoxycarbonyl-3-oxo-3-phenylpropyl)amino acid derivs.)

L18 ANSWER 9 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 126:31356 MARPAT
TITLE: Preparation of carboxylic .alpha.-N-sulfino cyclic anhydrides as ACE inhibitor intermediates
INVENTOR(S): Serra Mortes, Sonia; Palomo Coll, Alberto; Zupet, Rok
PATENT ASSIGNEE(S): Centro Genesis Para La Investigacion, S.L., Spain; Serra Mortes, Sonia; Palomo Coll, Alberto; Zupet, Rok
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9633984	A1	19961031	WO 1996-SI9	19960422
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
CA 2203435	AA	19961031	CA 1996-2203435	19960422
AU 9652944	A1	19961118	AU 1996-52944	19960422
PRIORITY APPLN. INFO.:			SI 1995-140	19950424
			WO 1996-SI9	19960422

OTHER SOURCE(S): CASREACT 126:31356
GI



I

AB Title compds. [I; R1 = CH2CH2Ph, or Pr; R2 = Me or (CH2)3NHR3; R3 = amino-protective group] were prepd. as intermediates in the synthesis of ACE inhibitors, esp. of enalapril and trandolapril. Thus, imidazole was chlorosulfinated with SOCl2 and the product used in situ to sulfinate N-[(S)-1-ethoxycarbonyl-3-phenylpropyl]-L-alanine to give I (R1 = CH2CH2Ph, R2 = Me). The latter was amidated in situ by silylated L-proline to give enalapril.

IC ICM C07D291-04
ICS A61K031-41; C07D207-16; C07D209-42; A61K031-40; C07K005-06
CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 34
ST carboxylic sulfino anhydride ACE inhibitor intermediate
IT 184346-33-6P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of carboxylic .alpha.-N-sulfino cyclic anhydrides as ACE inhibitor intermediates)
IT 76095-16-4P, Enalapril maleate 108449-50-9P 184346-34-7P
184489-54-1P 184489-55-2P 184489-56-3P 184489-57-4P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of carboxylic .alpha.-N-sulfino cyclic anhydrides as ACE inhibitor intermediates)
IT 147-85-3, L-Proline, reactions 80875-98-5 82717-96-2
145438-94-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of carboxylic .alpha.-N-sulfino cyclic anhydrides as ACE inhibitor intermediates)

L18 ANSWER 10 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 125:34172 MARPAT
TITLE: Preparation of angiotensin converting enzyme inhibitors.
INVENTOR(S): Serra Mortes, Sonia; Palomo Coll, Alberto; Zupet, Rok
PATENT ASSIGNEE(S): Lek, Tovarna Farmacevtskih in Kemicnih Izedlkov, D. D., Slovenia
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9602564	A1	19960201	WO 1995-SI17	19950713
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SK, TJ, TM, TT, UA, US, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2170872	AA	19960201	CA 1995-2170872	19950713
AU 9529424	A1	19960216	AU 1995-29424	19950713
EP 719280	A1	19960703	EP 1995-925228	19950713
EP 719280	B1	19991110		
R: GB				
US 5789597	A	19980804	US 1996-596214	19960215
PRIORITY APPLN. INFO.:			SI 1994-290	19940713
			SI 1994-450	19941221
			WO 1995-SI17	19950713

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds.(I; R = Q1-Q4, etc.), were prepd. by treatment of I (R = OH) (II)with ClSCOR1 or R1SOR1 (R1 = heterocyclyl such as imidazolyl, benzimidazolyl, 2-methylimidazolyl, triazolyl) to give intermediates (III) or (IV), which were reacted with (preferably silylated) amino acids. Thus, II was added to a soln. prepd. from SOCl2 and imidazole in CH2Cl2 and the mixt. was stirred at -15 to 20.degree.; the mixt. was filtered and treated with a soln. prepd. from Me3SiCl, proline, and Et3N in CH2Cl2. Solvent was removed and the residue was treated with aq. NaCl, EtOAc, and 35% HCl; the sepd. org. phase was treated with maleic acid to give 81.4% enalapril maleate.

IC ICM C07K005-02
ICS C07K233-61

CC 34-3 (Amino Acids, Peptides, and Proteins)

ST enalapril prepn; diquinalapril prepn; angiotensin converting enzyme inhibitor prepn

IT Peptides, preparation
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(analogs, prepn. of angiotensin converting enzyme inhibitors)

IT 151387-05-2P
RL: BYP (Byproduct); PREP (Preparation)
(prepn. of angiotensin converting enzyme inhibitors)

IT 76095-16-4P, Enalapril maleate 138332-08-8P, Enalapril hydrochloride 149404-21-7P, Enalapril sodium 177696-02-5P 177696-03-6P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of angiotensin converting enzyme inhibitors)

IT 147-85-3, Proline, reactions 77497-95-1 82717-96-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of angiotensin converting enzyme inhibitors)

IT 7364-47-8P 82006-94-8P 129258-49-7P 177545-70-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of angiotensin converting enzyme inhibitors)

L18 ANSWER 11 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 118:154603 MARPAT
TITLE: Method of treating premenstrual syndrome by administration of an angiotensin-converting enzyme inhibitor
INVENTOR(S): DePadova, Anthony Salvator
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9302679	A1	19930218	WO 1992-US6210	19920803

W: AU, CA, JP
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE

AU 9224139	A1	19930302	AU 1992-24139	19920803
PRIORITY APPLN. INFO.:			US 1991-740557	19910805
			WO 1992-US6210	19920803

AB A method of treating premenstrual syndrome is described which comprises the administration of a daily dose of an effective amt. of an angiotensin-converting enzyme inhibitor, e.g. quinapril, to a female of menstrual age. Tablet formulations of quinapril-HCl are included.
IC ICM A61K031-475
ICS A61K031-40; A61K031-675
CC 63-6 (Pharmaceuticals)
ST premenstrual syndrome angiotensin converting enzyme inhibitor; tablet quinapril hydrochloride premenstrual syndrome
IT Ovarian cycle
(disorder, premenstrual syndrome, treatment of, pharmaceutical compn. contg. angiotensin-converting enzyme inhibitor for)
IT Pharmaceutical dosage forms
(tablets, of quinapril hydrochloride,for premenstrual syndrome treatment)
IT 9015-82-1, Angiotensin-converting enzyme
RL: BIOL (Biological study)
(inhibitors of, pharmaceutical compn. contg., for premenstrual syndrome treatment)
IT 62571-86-2, Captopril 74258-86-9, Alacepril 75847-73-3, Enalapril 76547-98-3, Lisinopril 80876-01-3, Indolapril 81872-10-8, Zofenopril 82586-55-8, Quinapril hydrochloride 82834-16-0, Perindopril 82924-03-6, Pentopril 83435-66-9, Delapril 83647-97-6, Spirapril 85441-61-8, Quinapril 86541-75-5 87333-19-5, Ramipril 88768-40-5, Cilazapril 98048-97-6, Fosinopril 109214-55-3, Libenzapril
RL: BIOL (Biological study)
(pharmaceutical compn. contg., for premenstrual syndrome treatment)

L18 ANSWER 12 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 117:172104 MARPAT
TITLE: Methods for the synthesis of aminosuberic acid derivatives
INVENTOR(S): Hoffmann, Gerhard; Liedtke, Bernhard; Vollmer, Karl Otto
PATENT ASSIGNEE(S): Goedecke AG, Germany
SOURCE: Ger. Offen., 6 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4037960	A1	19920604	DE 1990-4037960	19901129
PRIORITY APPLN. INFO.:			DE 1990-4037960	19901129

OTHER SOURCE(S): CASREACT 117:172104
GI For diagram(s), see printed CA Issue.
AB Aminosuberic acid derivs. I (R1 = alkyl or alkenyl with up to 6 carbon atoms, C5-7-cycloalkyl, C5-7-cycloalkenyl,

C7-12-cycloalkylalkyl, C6-10-aryl, C7-14-aralkyl, mono- or bicyclic heterocyclic group; R2 = aryl; R3 = C1-6-alkyl, C2-6-alkenyl, C7-14-aralkyl; Z forms a heterocyclic ring) were prepd. by the selective cleavage of PhCH2O2CCHR1NHCH(CO2R3)CH2COR2 with AlCl3, condensing the resulting HO2CCHR1NHCH(CO2R3)CH2COR2 with heterocyclic compd. II, and hydrogenating the resulting ketone III with H2, deuterium or tritium. Thus, (S,S)-PhCOCH2CH(CO2Et)-Ala-OCH2Ph was debenzylated with AlCl3 in the presence of anisole in CH2Cl2/MeNO2 to give 86% (S,S)-PhCOCH2CH(CO2Et)-Ala-OH, which was condensed with (S)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid benzyl ester by DCC/1-hydroxybenzotriazole in CH2Cl2 to give product IV (isolated as the HCl salt). IV was hydrogenated over Pd/C in the presence of HCl to give 88% tetrahydroisoquinoline V.HCl.

IC ICM C07H005-06
ICS C07D217-26

CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

ST aminosuberic acid; suberic acid amino

IT 77497-96-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(coupling of, with alanine deriv.)

IT 87269-98-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(debenzylation of)

IT 143442-61-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and conversion of, to hydrochloride salt)

IT 87269-99-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and coupling of, with tetrahydroisoquinolinecarboxylic acid benzyl ester)

IT 143381-50-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydrogenation or deuteration of)

IT 82586-55-8P 143381-51-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and sapon. of)

IT 3054-07-7DP, 2-Aminosuberic acid, derivs. 82768-85-2P
143381-52-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L18 ANSWER 13 OF 17 MARPAT COPYRIGHT 2003 ACS

ACCESSION NUMBER: 117:143453 MARPAT

TITLE: Use of a combination of an ACE (angiotensin-converting enzyme) inhibitor with a calcium antagonist in the treatment of proteinuria

INVENTOR(S): Becker, Reinhard; Henning, Rainer; Teetz, Volker; Urbach, Hansjoerg

PATENT ASSIGNEE(S): Hoechst A.-G., Germany

SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 488059	A2	19920603	EP 1991-119892	19911121
EP 488059	A3	19921125		
EP 488059	B1	19950906		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
EP 649654	A1	19950426	EP 1994-117179	19911121
EP 649654	B1	19990210		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ES 2079545	T3	19960116	ES 1991-119892	19911121
AT 176592	E	19990215	AT 1994-117179	19911121
ES 2129563	T3	19990616	ES 1994-117179	19911121
AU 9188117	A1	19920528	AU 1991-88117	19911126
AU 655784	B2	19950112		
CA 2055948	AA	19920528	CA 1991-2055948	19911126
NO 9104637	A	19920529	NO 1991-4637	19911126
ZA 9109318	A	19920826	ZA 1991-9318	19911126
JP 04308533	A2	19921030	JP 1991-310608	19911126
HU 62468	A2	19930528	HU 1991-3674	19911126
HU 219447	B	20010428		
CN 1072601	A	19930602	CN 1991-111099	19911126
CN 1060679	B	20010117		
US 5236933	A	19930817	US 1991-798501	19911126
SK 279626	B6	19990111	SK 1991-3587	19911126
CZ 286168	B6	20000216	CZ 1991-3587	19911126
US 5366994	A	19941122	US 1993-57516	19930506
CZ 286187	B6	20000216	CZ 1997-2830	19970908
HK 1011927	A1	20000728	HK 1998-98113023	19981209
PRIORITY APPLN. INFO.:			DE 1990-4037691	19901127
			EP 1991-119892	19911121
			CS 1991-3587	19911126
			US 1991-798501	19911126

AB An ACE inhibitor R3O2CCHR4NR5C(:O)CHR1NHCH(CO2R2)(CH2)nR [n = 1, 2; R = H, (substituted) aliph., alicyclic, arom., hydrocarbyl- or heterocyclyloxy or -thio; R1 = H, (substituted) hydrocarbyl or heteroarom.; R2, R3 = H, (substituted) aliph., alicyclic, arom., araliph.; R4 and R5 complete a heterocyclic mono-, bi-, or tricyclic ring system with 3-15 C atoms], combined with a Ca antagonist, is used for prevention and therapy of proteinuria secondary to diabetes mellitus, glomerulosclerosis, and loss of kidney mass. Thus, rats with 1 kidney removed and the other infarcted through ligation were administered ramipril (ACE inhibitor; 1.4 mg/kg) and felodipine (Ca antagonist; 41 mg/kg) in the feed. An increase in proteinuria from <20 to 105 mg/24 h was obsd. in controls, compared to only 31 mg/24 h in treated rats. Tablets were prepd. contg. trandolapril (ACE inhibitor) 3, verapamil (Ca antagonist) 50, corn starch 130, gelatin 8.0, microcryst. cellulose 2.0, and Mg stearate 2.0 g/1000.

IC ICM A61K037-64
ICS A61K045-06

ICI A61K037-64, A61K031-135; A61K037-64, A61K031-44; A61K037-64, A61K031-55

CC 1-8 (Pharmacology)
Section cross-reference(s): 63

ST angiotensin converting enzyme inhibitor proteinuria; calcium antagonist proteinuria treatment

IT Proteins, biological studies
RL: BIOL (Biological study)
(metabolic disorders, proteinuria, treatment of, with angiotensin-converting enzyme inhibitor and calcium antagonist)
IT 7440-70-2, Calcium, biological studies
RL: BIOL (Biological study)
(antagonist of, proteinuria treatment with angiotensin-converting enzyme inhibitor and)
IT 9015-82-1, Angiotensin-converting enzyme
RL: BIOL (Biological study)
(inhibitor of, proteinuria treatment with calcium antagonist and)
IT 119884-28-5 119920-75-1 119920-79-5 143375-98-8 143375-99-9 143376-00-5 143376-01-6
RL: BIOL (Biological study)
(proteinuria treatment with)
IT 52-53-9, Verapamil 21829-25-4, Nifedipine 42399-41-7
RL: BIOL (Biological study)
(proteinuria treatment with angiotensin-converting enzyme inhibitor and)
IT 91-21-4D, derivs. 123-75-1D, Pyrrolidine, derivs. 172-62-3D, derivs. 175-94-0D, 2-Azaspiro[4.4]nonane, derivs. 176-66-9D, 2-Azaspiro[4.5]decane, derivs. 504-78-9D, Thiazolidine, derivs. 4375-14-8D, Octahydroindole, derivs. 5661-02-9D, derivs. 5661-03-0D, derivs. 6329-61-9D, Decahydroisoquinoline, derivs. 7140-62-7D, Decahydrocyclohepta[b]pyrrole, derivs. 21850-12-4D, derivs. 27202-71-7D, 2-Azabicyclo[3.1.0]hexane, derivs. 62571-86-2, Captopril 73263-16-8D, Spiro[(bicyclo[2.2.2]octane)-2,3'-pyrrolidine], derivs. 74258-86-9, Alacepril 75847-73-3, Enalapril 76547-98-3, Lisinopril 81872-10-8, Zofenopril 82834-16-0 83435-66-9, Delapril 83647-97-6, Spirapril 84768-09-2 85441-61-8, Quinapril 85856-54-8, Moveltipril 86541-75-5, Benazepril 87333-19-5, Ramipril 87679-37-6, Trandolapril 88768-40-5 89371-37-9 90130-77-1, S 9650 98048-97-6, Fosinopril 103775-10-6, Moexipril 109214-55-3, Libenzapril 109683-61-6, FPL 63547 110221-44-8 111223-26-8, Ceranapril 143384-22-9D, derivs. 143442-70-0D, derivs. 144275-78-5D, derivs.
RL: BIOL (Biological study)
(proteinuria treatment with calcium antagonist and)

L18 ANSWER 14 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 114:88663 MARPAT
TITLE: Combinations of angiotensin-converting enzyme (ACE) inhibitor and carbonic anhydrase (CA) inhibitor for treating glaucoma
INVENTOR(S): Lotti, Victor J.; Baldwin, John J.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 375299	A1	19900627	EP 1989-313161	19891215

R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE

CA 2005754	AA	19900619	CA 1989-2005754	19891218
DK 8906412	A	19900620	DK 1989-6412	19891218
JP 02212425	A2	19900823	JP 1989-329369	19891219
PRIORITY APPLN. INFO.:			US 1988-285932	19881219

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The ACE inhibitors are carboxylates RCHR5COACO2R6 [A = Q, Q1, Q2, Q3; R = R2CH2CR4(CO2R3)NH, HSCH2; R1, R3, R4, R6 = H, alkyl; R2 = alkyl, PhCH2, PhO, PhS, PhCH2O; R5 = R1, aminoalkyl; p, q = 0-2; r = 1, 2]. The CA inhibitors are sulfonamides I (R7 = H, R8 = Q4; or R7R8 = Q5, Q6, etc.; R9, R10 = H, alkyl; R11 = H, alkanoyl; R12 = alkoxyalkyl; R13 = H, alkoxyalkoxyalkyl). Compns. comprising an ACE inhibitor and a CA inhibitor are synergistic ophthalmic drugs for the treatment of glaucoma (no data).

IC ICM A61K037-64
ICS A61K009-06

ICI A61K037-64, A61K031-38

CC 63-6 (Pharmaceuticals)

ST glaucoma synergism drug enzyme inhibitor; angiotensin converting enzyme inhibitor glaucoma; carbonic anhydrase inhibitor glaucoma

IT Glaucoma (disease)
(treatment of, synergistic drugs contg. angiotensin-converting enzyme inhibitors and carbonic anhydrase inhibitors for)

IT 63250-36-2D, mixts. with carbonic anhydrase inhibitors
76391-23-6D, mixts. with carbonic anhydrase inhibitors
83601-86-9D, mixts. with carbonic anhydrase inhibitors
119731-42-9D, mixts. with angiotensin-converting enzyme inhibitors
122266-90-4D, mixts. with angiotensin-converting enzyme inhibitors
128620-92-8D, mixts. with angiotensin-converting enzyme inhibitors
131898-30-1D, mixts. with carbonic anhydrase inhibitors
RL: BIOL (Biological study)
(for glaucoma treatment, synergistic)

IT 9001-03-0, Carbonic anhydrase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, mixts. with angiotensin-converting enzyme inhibitors, synergistic, for glaucoma treatment)

IT 9015-82-1, Angiotensin-converting enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, mixts. with carbonic anhydrase inhibitors, synergistic, for glaucoma treatment)

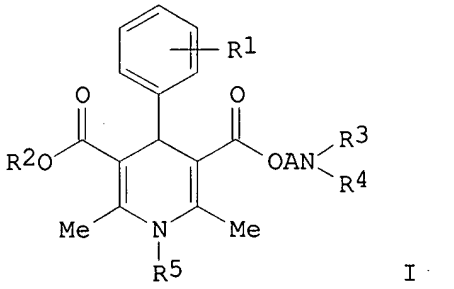
L18 ANSWER 15 OF 17 MARPAT COPYRIGHT 2003 ACS

ACCESSION NUMBER:	111:120883 MARPAT
TITLE:	Antihypertensive pharmaceuticals containing 1,4-dihydropyridine-3,5-dicarboxylic acid analogs and isoquinoline carboxylic acid analogs
INVENTOR(S):	Strosberg, Arthur M.; Whiting, Roger L.
PATENT ASSIGNEE(S):	Syntex (U.S.A.), Inc., USA
SOURCE:	Eur. Pat. Appl., 13 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

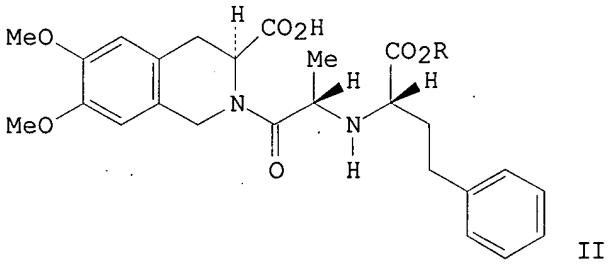
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 259838	A2	19880316	EP 1987-113121	19870908
EP 259838	A3	19891115		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DK 8704690	A	19880310	DK 1987-4690	19870908
AU 8778157	A1	19880317	AU 1987-78157	19870908
JP 63079831	A2	19880409	JP 1987-225141	19870908
ZA 8706716	A	19890426	ZA 1987-6716	19870908
PRIORITY APPLN. INFO.:			US 1986-905361	19860909

GI



I



II

AB Pharmaceuticals contain 2,6-dimethyl-4-phenyldihydropyridine-3,5-dicarboxylic acid derivs. (I; R1 = o- or m-substituted NO2, CF3, halo; R2 = alkyl, CH2CH2OMe; A = alkylene; R3 = alkyl, alkoxy, or optionally substituted Ph, or phenylalkyl; R4, R5 = H, alkyl) or salts of I, and an isoquinolinecarboxylic acid deriv. (II; R = H, alkyl) or salts of II. Antihypertensive tablets contained 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylic acid-3-Me ester-5-.beta.-(N-benzyl-N-methylamino)-Et ester (nicardipine) (III) (10 mg) and 2-[2-[(1-methoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl-1,2,3,4-tetrahydro-6,7-dimethoxy-3-isoquinolinecarboxylic acid (IV) (20 mg), corn starch (20 mg) spray-dried lactose (153 mg), and Mg stearate (2 mg). A combination of III (3 mg/kg orally) and IV (10 mg/kg orally) induced a greater antihypertensive effect on renal hypertensive rats with a systolic blood pressure >160 mmHg than did III or IV alone; the potentiation effect lasted >4 h.

IC ICM A61K031-47

Searcher : Shears 308-4994

ICI A61K031-47, A61K031-44
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
ST pyridine isoquinolinecarboxylate antihypertensive; calcium channel blocker antihypertensive
IT Antihypertensives
(calcium channel blocker-angiotensin-converting enzyme inhibitor mixts. as)
IT Ion channel blockers
(calcium, mixts. with angiotensin-converting enzyme inhibitors, as antihypertensive agents)
IT 122441-13-8
RL: BIOL (Biological study)
(antihypertensive agent)
IT 55985-32-5D, mixts. with isoquinolinecarboxylate analogs
122379-46-8D, mixts. with dihydropyridine analogs
RL: BIOL (Biological study)
(antihypertensive agents)
IT 9015-82-1, Angiotensin-converting enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, mixts. with calcium channel blockers, as antihypertensive agents)

L18 ANSWER 16 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 110:141552 MARPAT
TITLE: Pharmaceuticals containing angiotensin-converting enzyme inhibitors and ascorbates as stabilizers
INVENTOR(S): Murthy, Kuchi Sury; Harris, Michael Ray; Hokanson, Gerard Clifford; Reisch, Robert George, Jr.; Fawzi, Mahdi Bakir; Waldman, Frank Stanley
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 264887	A1	19880427	EP 1987-115281	19871019
EP 264887	B1	19910911		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 4830853	A	19890516	US 1986-921717	19861020
CA 1297024	A1	19920310	CA 1987-547231	19870918
ZA 8707132	A	19890426	ZA 1987-7132	19870922
AU 8779397	A1	19880421	AU 1987-79397	19871006
AU 604061	B2	19901206		
DK 8705435	A	19880421	DK 1987-5435	19871016
FI 8704594	A	19880421	FI 1987-4594	19871019
NO 8704352	A	19880421	NO 1987-4352	19871019
JP 63104931	A2	19880510	JP 1987-261931	19871019
JP 2703906	B2	19980126		
AT 67090	E	19910915	AT 1987-115281	19871019
ES 2040726	T3	19931101	ES 1987-115281	19871019
PRIORITY APPLN. INFO.:			US 1986-921717	19861020

EP 1987-115281 19871019

AB Pharmaceuticals contain an angiotensin converting-enzyme (ACE) inhibitor which is susceptible to discoloration, ascorbic acid (I) and/or Na ascorbate as color stabilizing agent(s), and optionally other additives. A formulation contained quinapril 5, I 20, lactose 71, and hydrogenated vegetable oil 4% by wt. This compn. was stable at 80% relative humidity for .gtoreq.24 h.

IC ICM A61K031-44
ICS A61K031-40; A61K047-00

CC 63-6 (Pharmaceuticals)

ST angiotensin converting enzyme inhibitor ascorbate; antihypertensive ascorbate

IT Discoloration prevention
(of angiotensin-converting enzyme inhibitor-contg. pharmaceuticals, ascorbates for)

IT 9015-82-1, Angiotensin converting enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, pharmaceuticals contg. ascorbates and)

IT 50-81-7, Ascorbic acid, biological studies 134-03-2, Sodium ascorbate
RL: BIOL (Biological study)
(pharmaceuticals contg. antihypertensive angiotensin-converting enzyme inhibitors and)

IT 75847-73-3, Enalapril 82768-84-1 85441-61-8, Quinapril 103775-10-6
RL: BIOL (Biological study)
(pharmaceuticals contg. ascorbates and)

L18 ANSWER 17 OF 17 MARPAT COPYRIGHT 2003 ACS

ACCESSION NUMBER: 109:48448 MARPAT

TITLE: Neutral metalloendopeptidase inhibitors in the treatment of hypertension, compositions and kits containing the inhibitors, manufacture of the compositions, compounds of the compositions and their preparation

INVENTOR(S): Haslanger, Martin F.; Sybertz, Edmund, Jr.; Neustadt, Bernard R.; Smith, Elizabeth M.

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: Eur. Pat. Appl., 167 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 254032	A2	19880127	EP 1987-108730	19870617
EP 254032	A3	19900905		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 4749688	A	19880607	US 1986-876610	19860620
US 4801609	A	19890131	US 1987-32153	19870327
EP 566157	A1	19931020	EP 1993-107499	19870617
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FI 8702720	A	19871221	FI 1987-2720	19870618
AU 8774458	A1	19871224	AU 1987-74458	19870618
AU 602701	B2	19901025		
ZA 8704413	A	19880224	ZA 1987-4413	19870618

HU 44940	A2	19880530	HU 1987-2786	19870618
IL 82908	A1	19910916	IL 1987-82908	19870618
DK 8703138	A	19871221	DK 1987-3138	19870619
NO 8702589	A	19871221	NO 1987-2589	19870619
JP 63039855	A2	19880220	JP 1987-153219	19870619
JP 2542620	B2	19961009		
JP 08283153	A2	19961029	JP 1995-246555	19870619
US 5061710	A	19911029	US 1987-133669	19871216
AU 9068517	A1	19910718	AU 1990-68517	19901227
AU 636423	B2	19930429		
US 4801609	B1	19931109	US 1991-90002282	19910214
US 5262436	A	19931116	US 1991-741025	19910806
JP 08176100	A2	19960709	JP 1995-246554	19950821
PRIORITY APPLN. INFO.:			US 1986-876610	19860620
			US 1987-32153	19870327
			EP 1987-108730	19870617
			JP 1987-153219	19870619
			US 1987-133669	19871216

AB Neutral metalloendopeptidase (NMEP) inhibitor is used alone or combined with an atrial peptide or an angiotensin converting enzyme (ACE) inhibitor for prepn. of pharmaceutical compns. for treating hypertension. The compns. are obtained by mixing a NMEP inhibitor, alone or combined with an atrial peptide or ACE inhibitor, with a pharmaceutically acceptable carrier. S-(4-Methylbenzyl)-L-cysteine, Me ester hydrochloride was prepd. by adding thionyl chloride dropwise to N-tert-butyloxycarbonyl-S-(4-methylbenzyl)-L-cysteine in MeOH, heating the mixt. under reflux for 90 min, cooling to room temp., and concg. in vacuo. Rats with induced hypertension were dosed s.c. with N-(N-[L-1-(2,2-dimethyl-1-oxopropoxy)methoxy]carbonyl)-2-phenylethyl)-L-phenylalanine]-.beta.-alanine and 1-[(2S)-3-mercapto-2-methyl-1-oxypropyl]-L-proline in Me cellulose vehicle to give a 1-, 2-, 3-, and 4-h decrease in blood pressure of 14, 19, 19, and 15 mMHg vs. an increase of 14, 11, 11, and 8 with the NMEP inhibitor alone and a decrease of 11, 7, 1, and 1 mMHg with the ACE inhibitor alone.

IC ICM A61K037-64

CC 1-8 (Pharmacology)
Section cross-reference(s): 34, 63

ST NMEP inhibitor atrial peptide antihypertensive

IT Antihypertensives
(neutral metalloendopeptidase inhibitors and angiotensin converting enzyme inhibitors or atriopeptins as)

IT 62571-86-2, Captopril 75847-73-3 76547-98-3, Lysinopril 80876-01-3, Indolapril 81045-50-3, Pivalopril 81872-10-8, Zofenopril 82834-16-0, Perindopril 82924-03-6, Pentopril 83647-97-6, Spirapril 87333-19-5, Ramipril 88768-40-5, Cilazapril
RL: BIOL (Biological study)
(angiotensin converting enzyme inhibitor, antihypertensive contg. neutral metalloendopeptidase inhibitor and)

IT 82586-52-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(angiotensin converting enzyme inhibitor, antihypertensive contg. neutral metalloendopeptidase inhibitor and)

IT 115156-91-7 115156-92-8 115156-94-0
RL: BIOL (Biological study)
(angiotensin converting enzyme inhibitor-neutral

metalloendopeptidase inhibitor mixt., with antihypertensive properties)

IT 88898-17-3 89139-53-7, Atriopeptin-21 (rat) 89139-54-8
89213-87-6 89944-37-6, Atriopeptin-33 (rat) 90052-57-6
90817-13-3 90984-99-9 94705-21-2, Atriopeptin 33 (human)
95896-08-5 98897-20-2 98929-56-7 98929-57-8 102686-43-1
RL: BIOL (Biological study)
(antihypertenive pharmaceuticals contg. neutral metalloendopeptidase inhibitors and)

IT 82707-54-8
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, antihypertensive compns. contg. atriopeptins or angiotensin converting enzyme inhibitors and)

IT 9015-82-1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, pharmaceuticals with neutral metalloendopeptidase inhibitor, with antihypertensive properties)

IT 83861-02-3 95198-45-1 105368-09-0 115156-93-9 115355-20-9
115355-21-0 115355-22-1
RL: BIOL (Biological study)
(neutral metalloendopeptidase inhibitor, antihypertensive contg.)

IT 83825-63-2 83861-02-3 95176-40-2 95198-15-5 95198-52-0
115156-93-9 115355-21-0 115355-22-1 115370-39-3 115370-40-6
115370-41-7 115370-42-8 115370-43-9 115370-44-0 115370-45-1
115370-46-2 115370-47-3 115370-48-4 115370-49-5 115370-50-8
115370-51-9 115370-52-0 115406-22-9 115406-23-0
RL: BIOL (Biological study)
(neutral metalloendopeptidase inhibitor, with antihypertensive properties)

IT 85637-73-6, Atriopeptin
RL: BIOL (Biological study)
(pharmaceuticals with neutral metalloendopeptidase inhibitors, with antihypertensive properties)

IT 2107-84-8P 27650-96-0P 95244-36-3P 105852-67-3P 115369-83-0P
115369-84-1P 115369-85-2P 115369-86-3P 115369-87-4P
115369-88-5P 115369-89-6P 115369-90-9P 115369-91-0P
115369-92-1P 115369-93-2P 115369-94-3P 115369-95-4P
115369-96-5P 115369-97-6P 115369-98-7P 115369-99-8P
115370-00-8P 115370-01-9P 115370-02-0P 115370-03-1P
115370-04-2P 115370-05-3P 115370-06-4P 115370-07-5P
115370-08-6P 115370-09-7P 115370-10-0P 115370-11-1P
115370-53-1P 115370-54-2P 115391-56-5P 115406-17-2P
115406-18-3P 115406-19-4P 115406-20-7P 115406-21-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in neutral metalloendopeptidase inhibitor prepn.)

IT 115370-12-2P 115370-13-3P 115370-14-4P 115370-15-5P
115370-16-6P 115370-17-7P 115370-18-8P 115370-19-9P
115370-20-2P 115370-21-3P 115370-22-4P 115370-23-5P
115370-24-6P 115370-25-7P 115370-26-8P 115370-27-9P
115370-28-0P 115370-29-1P 115370-30-4P 115370-31-5P
115370-32-6P 115370-33-7P 115370-34-8P 115370-35-9P
115370-36-0P 115370-37-1P 115370-38-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as neutral metalloendopeptidase inhibitor)

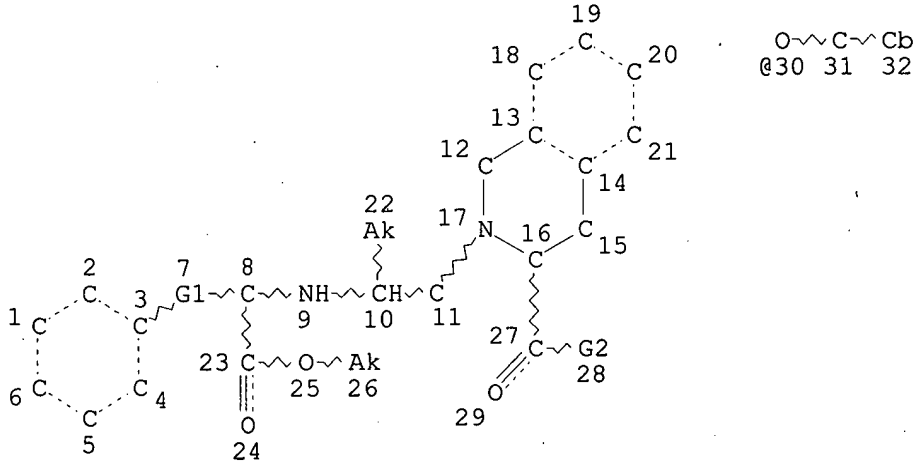
IT 13026-12-5P 34805-17-9P, O-Benzyl-L-tyrosine methyl ester hydrochloride 52844-67-4P 66076-76-4P 71449-22-4P

74401-75-5P 84952-45-4P 88389-36-0P 88424-57-1P 88660-34-8P
95260-87-0P 98574-43-7P 115355-23-2P 115355-24-3P
115355-25-4P 115355-26-5P 115355-27-6P 115355-28-7P
115355-29-8P 115355-30-1P 115355-31-2P 115355-32-3P
115355-33-4P 115355-34-5P 115355-35-6P 115355-36-7P
115355-37-8P 115355-38-9P 115355-39-0P 115355-40-3P
115355-41-4P 115355-42-5P 115355-43-6P 115355-44-7P
115355-45-8P 115355-46-9P 115355-47-0P 115355-48-1P
115355-49-2P 115355-50-5P 115355-51-6P 115355-52-7P
115355-53-8P 115355-54-9P 115355-55-0P 115355-56-1P
115355-57-2P 115369-78-3P 115369-79-4P 115369-80-7P
115405-37-3P 115405-38-4P 115405-39-5P 115405-40-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as neutral metalloendopeptidase inhibitor inhibitor)

IT 76-05-1, Trifluoroacetic acid, reactions 105-53-3 115-11-7, Isobutylene, reactions 121-44-8, Triethylamine, reactions 141-52-6, Sodium ethanolate 141-82-2, Malonic acid, reactions 507-09-5, Thioacetic acid, reactions 1535-57-5 2177-63-1 3163-27-7, .alpha.-Bromomethylnaphthalene 3218-36-8, 4-Biphenyl carboxaldehyde 4510-08-1, L-Methionine amide 6287-94-1 10332-17-9, Methionine methyl ester 13485-59-1, L-Alanyl-L-proline 14510-12-4 42294-52-0, S-(4-Methylbenzyl)-L-cysteine 52844-67-4 61925-77-7 80969-99-9 83024-49-1 84609-11-0 100484-62-6 115355-23-2 115355-30-1 115369-81-8 115369-82-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in neutral metalloendopeptidase inhibitor prepn.)

FILE 'MARPATPREV' ENTERED AT 12:08:31 ON 21 APR 2003

L16 STR



Searcher : Shears 308-4994

NUMBER OF NODES IS 32

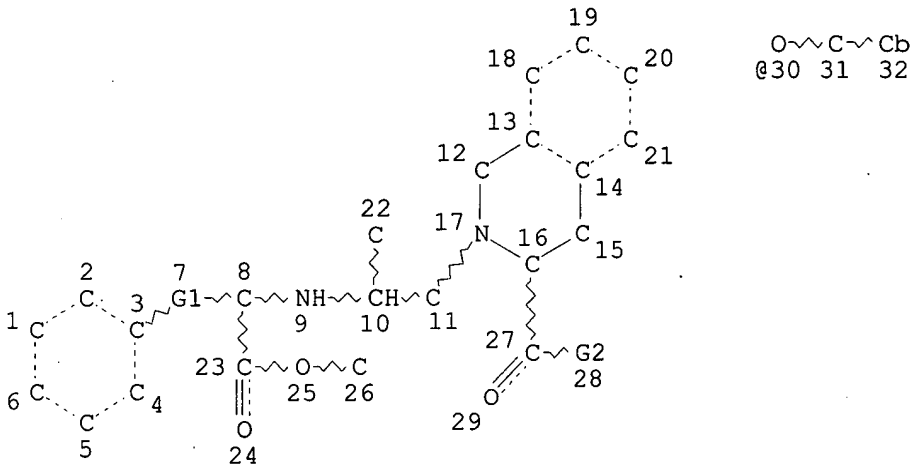
STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L19 0 SEA FILE=MARPATPREV SSS FUL L16 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 3 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

(FILE 'CASREACT' ENTERED AT 12:08:58 ON 21 APR 2003)
L21 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 32
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE
L23 4 SEA FILE=CASREACT SSS FUL L21 (32 REACTIONS)

100.0% DONE 211 VERIFIED 32 HIT RXNS 4 DOCS
SEARCH TIME: 00.00.01

L23 ANSWER 1 OF 4 CASREACT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 136:279699 CASREACT
TITLE: Preparation of amino acid salts soluble in organic solvents and their use in dipeptide synthesis
INVENTOR(S): Palomo Nicolau, Francisco Eugenio; Palomo Coll, Antonio Luis

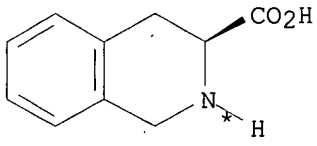
PATENT ASSIGNEE(S): Spain
SOURCE: Span., 23 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2156050	A1	20010601	ES 1998-753	19980331
ES 2156050	B1	20020316		

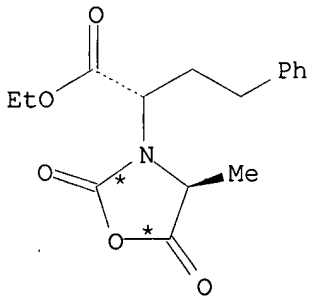
PRIORITY APPLN. INFO.: ES 1998-753 19980331
OTHER SOURCE(S): MARPAT 136:279699

AB .alpha.-Amino acids salts with org. super bases, R0CO2-A-NH-Q+-[N(B)D]n [Q = C (n = 1 or 2) or P (n = 3); A, B, D = alkyl, alkylaryl or may combine to form a heterocyclic group; R = H or a side chain of an amino acid; R0 is an aminohetero(bi)cyclic C5-C10 residue having one or two atoms O, S or N or a group R1NHCHR, where R = H or a side chain of an optionally protected amino acid, R1 = H, Ph3C; or R and R1 may combine to form a mono-, bi-, or tricyclic heterocyclic ring], which are sol. in org. solvents, were prepd. for use in the prepn. of dipeptides. Tetramethylformamidinium, benzotriazolylmethyl, and oxime active esters were used in this process. Thus, treatment of an acetonitrile soln. of L-proline and DBU with N-[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]-L-alanine O-acetone oxime (prepn. given) afforded 95% enalapril (isolated as the maleate).

RX(8) OF 13 AM + AN ===> **AO**

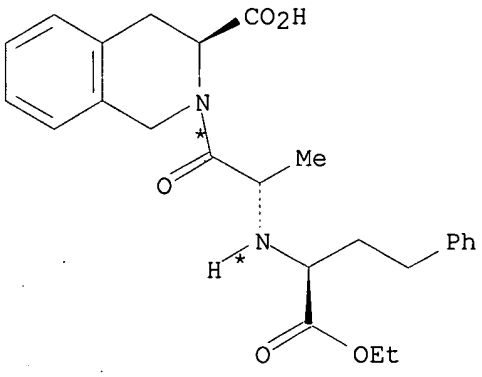


AM



AN

(8) ⟶



AO
YIELD 90%

RX(8) RCT AM 74163-81-8

STAGE(1)
RGT D 6674-22-2 DBU
SOL 75-05-8 MeCN

STAGE(2)
RGT AC 90825-38-0 Phosphorus(1+), ethyltris(N-ethylethanaminato)-, (T-4)-
SOL 75-09-2 CH2Cl2

STAGE(3)
SOL 75-09-2 CH2Cl2

STAGE(4)
RCT AN 84793-24-8
SOL 75-09-2 CH2Cl2
PRO AO **85441-61-8**

L23 ANSWER 2 OF 4 CASREACT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 135:288704 CASREACT
TITLE: Preparation of stable pharmaceutical formulations containing moexipril magnesium and the preparation of moexipril magnesium
INVENTOR(S): Sherman, Bernard Charles
PATENT ASSIGNEE(S): Can.
SOURCE: Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1142878	A2	20011010	EP 2001-302450	20010316

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,

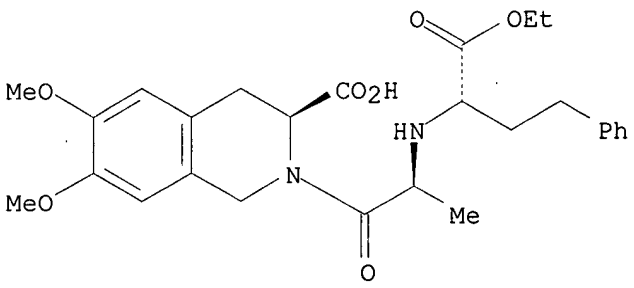
PT, IE, SI, LT, LV, FI, RO

US 2002037858 A1 20020328 US 2001-809173 20010316

PRIORITY APPLN. INFO.: CA 2000-2303481 20000405

AB Moexipril magnesium, a more stable form of moexipril, is prepd. by reacting moexipril or one of its acid-addn. salts (e.g., moexipril hydrochloride) with an alk. magnesium compd. (e.g., magnesium hydroxide) in the presence of a solvent (e.g., water and acetone) to convert most or all of the moexipril or the moexipril acid addn. salt into moexipril magnesium.

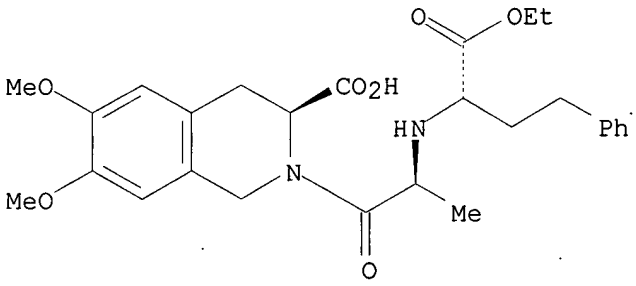
RX(1) OF 1 **A** ===> B



● HCl

A

(1) →



● 1/2 Mg

B

RX(1) RCT A **82586-52-5**
PRO B 365278-21-3
SOL 7732-18-5 Water, 67-64-1 Me2CO

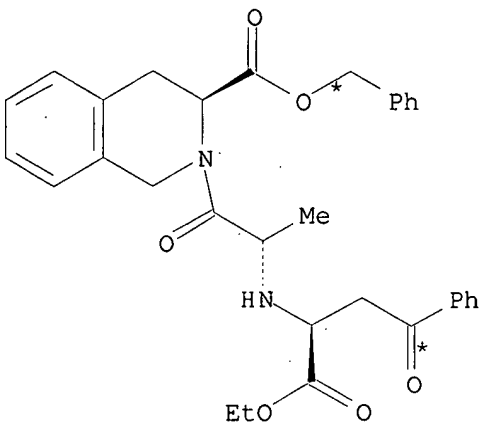
L23 ANSWER 3 OF 4 CASREACT COPYRIGHT 2003 ACS

ACCESSION NUMBER: 117:172104 CASREACT
TITLE: Methods for the synthesis of aminosuberic acid derivatives
INVENTOR(S): Hoffmann, Gerhard; Liedtke, Bernhard; Vollmer, Karl Otto
PATENT ASSIGNEE(S): Goedecke AG, Germany
SOURCE: Ger. Offen., 6 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4037960	A1	19920604	DE 1990-4037960	19901129

PRIORITY APPLN. INFO.: DE 1990-4037960 19901129
OTHER SOURCE(S): MARPAT 117:172104
GI For diagram(s), see printed CA Issue.
AB Aminosuberic acid derivs. I (R1 = alkyl or alkenyl with up to 6 carbon atoms, C5-7-cycloalkyl, C5-7-cycloalkenyl, C7-12-cycloalkylalkyl, C6-10-aryl, C7-14-aralkyl, mono- or bicyclic heterocyclic group; R2 = aryl; R3 = C1-6-alkyl, C2-6-alkenyl, C7-14-aralkyl; Z forms a heterocyclic ring) were prepd. by the selective cleavage of PhCH2O2CCHR1NHCH(CO2R3)CH2COR2 with AlCl3, condensing the resulting HO2CCHR1NHCH(CO2R3)CH2COR2 with heterocyclic compd. II, and hydrogenating the resulting ketone III with H2, deuterium or tritium. Thus, (S,S)-PhCOCH2CH(CO2Et)-Ala-OCH2Ph was debenzylated with AlCl3 in the presence of anisole in CH2Cl2/MeNO2 to give 86% (S,S)-PhCOCH2CH(CO2Et)-Ala-OH, which was condensed with (S)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid benzyl ester by DCC/1-hydroxybenzotriazole in CH2Cl2 to give product IV (isolated as the HCl salt). IV was hydrogenated over Pd/C in the presence of HCl to give 88% tetrahydroisoquinoline V.HCl.

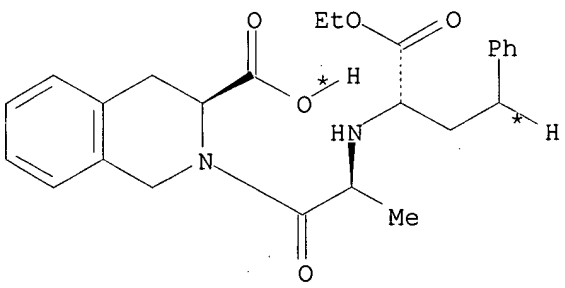
RX(3) OF 6 L ===> **M...**



● HCl

L

(3) →



● HCl

M
YIELD 60%

RX(3) RCT L 143381-50-4
RGT N 1333-74-0 H2, O 7647-01-0 HCl
PRO M **82586-55-8**
CAT 7440-05-3 Pd
SOL 60-29-7 Et2O

L23 ANSWER 4 OF 4 CASREACT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 105:208744 CASREACT
TITLE: Synthesis of novel angiotensin converting enzyme inhibitor quinapril and related compounds. A divergence of structure-activity relationships

Searcher : Shears 308-4994

for non-sulfhydryl and sulfhydryl types

AUTHOR(S): Klutchko, Sylvester; Blankley, C. John; Fleming, Robert W.; Hinkley, Jack M.; Werner, Ann E.; Nordin, Ivan; Holmes, Ann; Hoefle, Milton L.; Cohen, David M.; et al.

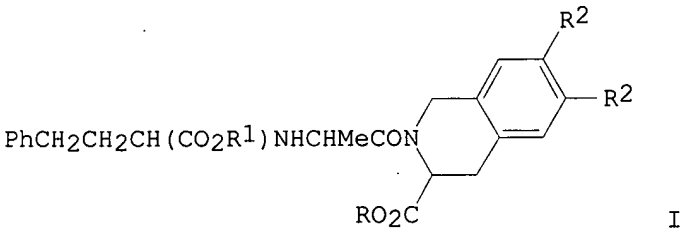
CORPORATE SOURCE: Dep. Chem., Warner-Lambert/Parke-Davis Pharm. Res., Ann Arbor, MI, 48106, USA

SOURCE: Journal of Medicinal Chemistry (1986), 29(10), 1953-61
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

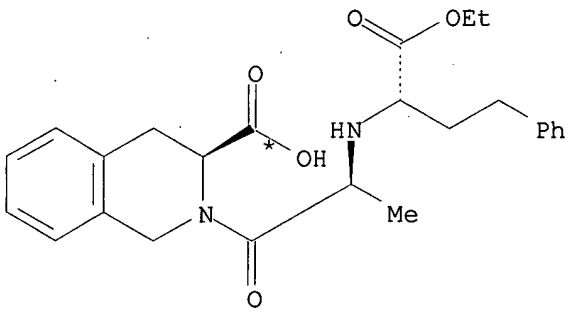
LANGUAGE: English

GI



I

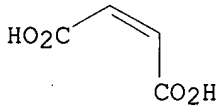
AB The synthesis and angiotensin-converting enzyme (ACE) inhibiting activities of quinapril (S,S,S)-I (R = R2 = H, R1 = Et), its active diacid (S,S,S)-I (R = R1 = R2 = H), and its dimethoxy analog (S,S,S)-I (R = H, R1 = Et, R2 = MeO) are reported. Thus, (S)-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid 1,1-dimethylethyl ester was acylated with (S,S)-PhCH2CH2CH(CO2Et)NHCHMeCO2H followed by hydrolysis of the product to give (S,S,S)-I (R = R2 = H, R1 = Et). These tetrahydro-3-isoquinolinecarboxylic acid derivs. possess in vitro potency and in vivo efficacy equiv. to that of enalapril. Sulfhydryl analogs with the same structural variation are also highly potent. In contrast, tetrahydro-1-isoquinolinecarboxylic acid and homologous isoindoline-1-carboxylic acid analogs show a striking divergence in potency between the two types, sulfhydryl analogs being essentially inactive, while non-sulfhydryl analogs are equipotent with the proline prototype. This is the first evidence suggesting that alternate binding modes may exist for the two major structural classes of small mol. ACE inhibitors.



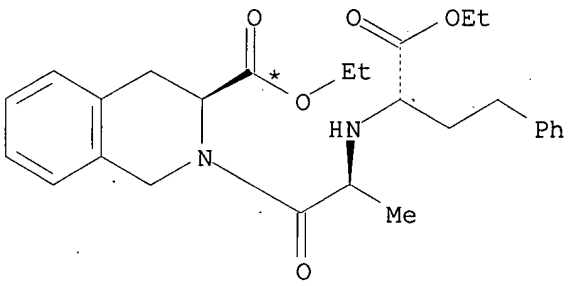
● HCl

T

(5) →



U: CM 1

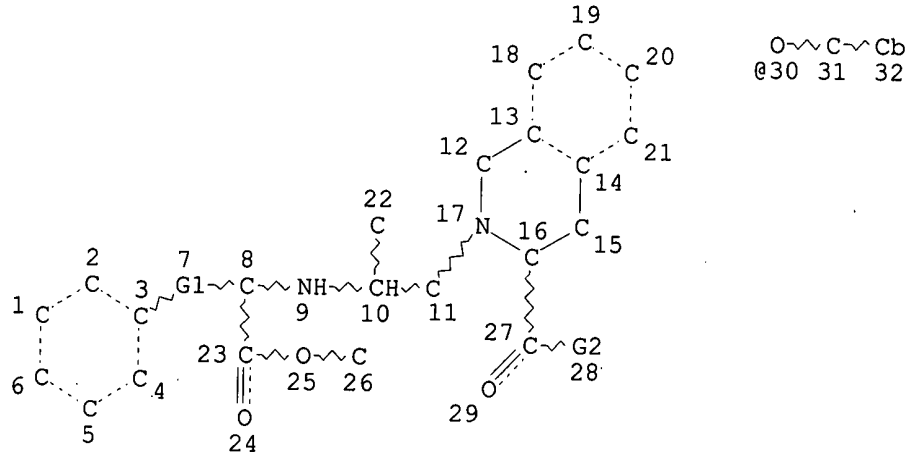


U: CM 2

RX(5) RCT T **82586-55-8**
RGT F 7647-01-0 HCl
PRO U 103733-36-4
SOL 64-17-5 EtOH

(FILE 'DJSMDS, CHEMINFORMRX, CHEMREACT' ENTERED AT 12:10:38 ON 21 APR 2003)

L21 STR



REP G1=(1-3) CH2
VAR G2=OH/30
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 32
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE
L24 0 SEA L21

FILE 'HOME' ENTERED AT 12:11:21 ON 21 APR 2003